

**TO DETECT CONTACT HYPERSENSITIVITY TO
COSMETICS IN PATIENTS WITH SCALP PRURITUS
BY PATCH TESTING**

Dissertation Submitted to

THE TAMILNADU DR. M.G.R. MEDICAL UNIVERSITY

In fulfillment of the regulations for the award of the degree

M.D.

DERMATOLOGY, VENEREOLOGY AND LEPROLOGY



**DEPARTMENT OF DERMATOLOGY, VENEROLOGY
AND LEPROLOGY**

**PSG INSTITUTE OF MEDICAL SCIENCE AND RESEARCH
THE TAMILNADU DR.M.G.R.MEDICAL UNIVERSITY
CHENNAI, TAMILNADU**

APRIL 2016

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GUIDE

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**THE TAMILNADU DR.M.G.R.MEDICAL UNIVERSITY
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APRIL 2016

CERTIFICATE

This is to certify that the thesis entitled **“TO DETECT CONTACT HYPERSENSITIVITY TO COSMETICS IN PATIENTS WITH SCALP PRURITUS BY PATCH TESTING”** is a bonafide work of **Dr.ANITA K.** done under the direct guidance and supervision of **Dr.C.R.SRINIVAS. MD**, in the department of Dermatology, Venereology and Leprology, PSG Institute of Medical Sciences and Research, Coimbatore in fulfillment of the regulations of Dr.MGR Medical University for the award of MD degree in Dermatology, Venereology and Leprology.

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DEAN

DECLARATION

I hereby declare that this dissertation entitled “ **TO DETECT CONTACT HYPERSENSITIVITY TO COSMETICS IN PATIENTS WITH SCALP PRURITIS BY PATCH TESTING** ” was prepared by me under the direct guidance and supervision of **DR. C.R. SRINIVAS, MD,** PSG Institute of Medical Sciences and Research, Coimbatore.

The dissertation is submitted to the Tamilnadu Dr.MGR Medical University in fulfillment of the University regulation for the award of MD degree in Dermatology, Venereology and Leprology. This dissertation has not been submitted for the award of any other Degree or Diploma.

DR. ANITA K.

CERTIFICATE BY THE GUIDE

This is to certify that the thesis entitled “ **TO DETECT CONTACT HYPERSENSITIVITY TO COSMETICS IN PATIENTS WITH SCALP PRURITIS BY PATCH TESTING** ” is a bonafide work of **DR. ANITA K.** done under my direct guidance and supervision in the department of Dermatology, Venereology and Leprology, PSG Institute of Medical Sciences and Research, Coimbatore in fulfillment of the regulations of Dr.MGR Medical University for the award of MD degree in Dermatology, Venereology and Leprology.

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Ref.: Study titled "To detect contact hypersensitivity to cosmetics in patients with allergic contact dermatitis of scalp by patch testing"

Sub.: Clarifications required

In the Institutional Human Ethics Committee meeting held on 16.06.2014, at Research Conference Room, PSG IMS&R, between 9.30 am and 12.30 pm, the documents related to the above proposal were reviewed and discussed.

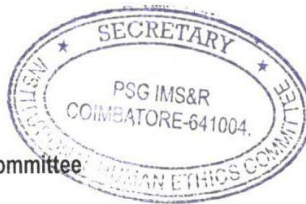
The following queries emerged during the discussion:

- Please submit assent form for the participants in the age group of 15 – 18 years

Decision: Approval pending for minor modifications

Kindly note that this is not the final approval letter and research participants cannot be recruited until the final approval is given.


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"Disseminated cutaneous aspergillosis presenting as granulomatous plaque in an immunocompetant patient"

The following documents were received for review:

1. Duly filled application form
2. Case Report
3. Confidentiality statement
4. Application for waiver of consent
5. CV

After due consideration, the Committee has decided to approve the above case report.

The members who attended the meeting, at which your case report was discussed, are listed below:

Name	Qualification	Responsibility in IHEC	Gender	Affiliation to the Institution Yes/No	Present at the meeting Yes/No
Dr P Sathyan	DO, DNB	Clinician, Chairperson	Male	No	Yes
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Dr Y S Sivan	Ph D	Member – Social Scientist	Male	Yes	Yes
Dr D Vijaya	Ph D	Member – Basic Scientist	Female	Yes	Yes

The approval is valid for one year.

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Yours truly,


for **Dr S Bhuvaneshwari**
Member – Secretary
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The Institutional Human Ethics Committee, PSG IMS & R, Coimbatore -4, has reviewed your proposal on 13th February, 2015 in its expedited review meeting held at IHEC Secretariat, PSG IMS&R, between 10.00 am and 11.00 am, and discussed your request to change the title of your study entitled:

"To detect contact hypersensitivity to cosmetics in patients with allergic contact dermatitis of scalp by patch testing"

The following documents were received for review:

1. Your letter dated 04.02.2015
2. Amendment reporting form
3. Informed consent form

After due consideration, the Committee has decided to approve the following:

1. Change of title as *"To detect contact hypersensitivity to cosmetics in patients with scalp pruritis by patch testing"*

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Dr S Bhuvaneshwari	M.D	Clinical Pharmacologist Member - Secretary	Female	Yes	Yes
Dr. S. Shanthakumari	MD	Pathology, Ethicist	Female	Yes	Yes
Dr D Vijaya	Ph D	Member - Basic Scientist	Female	Yes	Yes

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To detect contact hypersensitivity to cosmetics in patients with scalp pruritus by patch

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INTRODUCTION

Scalp pruritus is a common complaint we face, is diagnostically and therapeutically challenging situation. When we do not know an answer to a question we scratch our heads is a well known phenomenon, may be it stimulates the brain!. Scratching is a trick known to mothers to put us to sleep. But not all scalp pruritus is pleasant and it can be very disturbing. There are various causes of scalp pruritus, not only dermatological but can also be due to systemic causes.

Allergic contact dermatitis to cosmetics are mostly irritant in nature. Development of delayed type hypersensitivity due to cosmetics is rare and it depends on product composition, concentration of the allergen, sensitizing potential of the allergen, duration of exposure, penetration of the product and

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TO DETECT CONTACT HYPERSENSITIVITY TO COSMETICS IN PATIENTS WITH SCALP PRURITIS BY PATCH TESTING

Introduction

Scalp pruritis is a common presenting complaint that is considered a diagnostically and therapeutically challenging situation. Contact dermatitis of the scalp can occur primarily after application of cosmetic products on healthy skin or secondarily on skin affected by dermatosis such as seborrhoeic dermatitis, psoriasis etc. Active ingredients of hair care products have been found to be the third most common cause of allergic contact dermatitis.

Objective

To identify the common topical medicaments and cosmetics capable of producing scalp pruritus and value of patch testing in these situations.

Materials and methods

20 patients with history of scalp pruritis were patch tested with cosmetic series kit of chemotechnique diagnostics AB Sweden and in addition, patients own products were also tested. For wash off products like shampoos patch test was done at a concentration of 1:10. The reading was taken at 48hrs and 72hrs, and results interpreted according to the ICDRG criteria.

Results

Out of 20, 17 patients were positive for one or more allergens. Paraphenylenediamine (PPD) was found to be the most common allergen in 9 out of 20. Followed by gallate mix in 7 patients and cetrimonium bromide in 6 patients. And, 8 patients showed positivity for more than 2 allergens.

Conclusion

This study was undertaken to to identify allergens inducing pruritis of scalp by patch testing and to find the incidence of allergic contact dermatitis to topical preparations and cosmetics among patients with pruritis of scalp. We recommend patch testing in patients with long standing pruritis of scalp.

INTRODUCTION

Scalp pruritus is a common complaint we face, is diagnostically and therapeutically challenging situation. When we do not know an answer to a question we scratch our heads is a well known phenomenon, may be it stimulates the brain!. Scratching is a trick known to mothers to put us to sleep. But not all scalp pruritus is pleasant and it can be very disturbing. There are various causes of scalp pruritus, not only dermatological but can also be due to systemic causes.

Allergic contact dermatitis to cosmetics is mostly irritant in nature. Development of delayed type hypersensitivity due to cosmetics is rare and it depends on product composition, concentration of the allergen, sensitizing potential of the allergen, duration of exposure, penetration of the product and the application site.¹

Hair cosmetics like shampoos are used almost daily by many people. Scalp pruritus may develop primarily after application of cosmetics on healthy skin or secondarily due to cosmetics and topical used over a pre-existing dermatitis scalp which can cause aggravation.

Trüeb defines hair cosmetics as “preparations intended for placing in contact with the hair and scalp, with the purpose of cleansing, promoting attractiveness, altering appearance, and/or protecting them in order to maintain them in good condition.”²

Adverse reactions due to cosmetics are mainly due to four classes of ingredients preservatives, emulsifiers, fragrances and colouring agents. Among them fragrances are the most common cause followed by preservatives. Most of the individuals who develop a cutaneous reaction to cosmetic will have mild reaction so they simply discontinue the product. So the exact prevalence of cosmetic allergy cannot be estimated. Allergy to a product can occur immediately after application or after years of application. Ingredients in hair cosmetics are found to be the third most common source of allergic reactions in USA.

Patch testing is considered the gold standard for the diagnosis of allergic contact dermatitis. But not all allergens can be identified because the patch test series contains only the most common ones. As dermatologists we must be aware of the ingredients, principles of hair care products, formulations and side effects. The purpose is not only to diagnose and treat the disorder also to improve the psychological impact on the patient.

AIM

To identify the common topical medicaments and cosmetics capable of producing scalp pruritus by patch testing

REVIEW OF LITERATURE

PRURITUS

A simple definition of itch was first proposed by Samuel Hafenreffer 340 years ago as ‘an unpleasant sensation provoking the desire to scratch’³ Itching can be acute, chronic, intractable and alloknesis. Pruritus is a common manifestation of dermatologic conditions, increasing in incidence with age. In some patients itching is very severe and it impairs the quality of life.

TYPES OF ITCHING

Itching has been classified as it helps us to evaluate and treat itch in a more meaningful way.⁴

- 1. Pruritoceptive itch:** itching that originates in the skin due to inflammation, dryness, or other skin damage. Examples include Urticaria, Insect bite reactions, scabies, allergic contact dermatitis etc.,
- 2. Neuropathic itch:** itching due to a particular pathway located at any point along the afferent pathway. Examples include post herpetic itch, cerebral vascular events, brain tumors etc.,
- 3. Neurogenic itch:** itch that originates centrally without evidence of neural pathology. Eg- cholestasis.
- 4. Psychogenic itch:** itching due to psychological abnormalities. Examples include delusional parasitosis, compulsive disorders etc.,

PATHOPHYSIOLOGY OF PRURITUS⁵

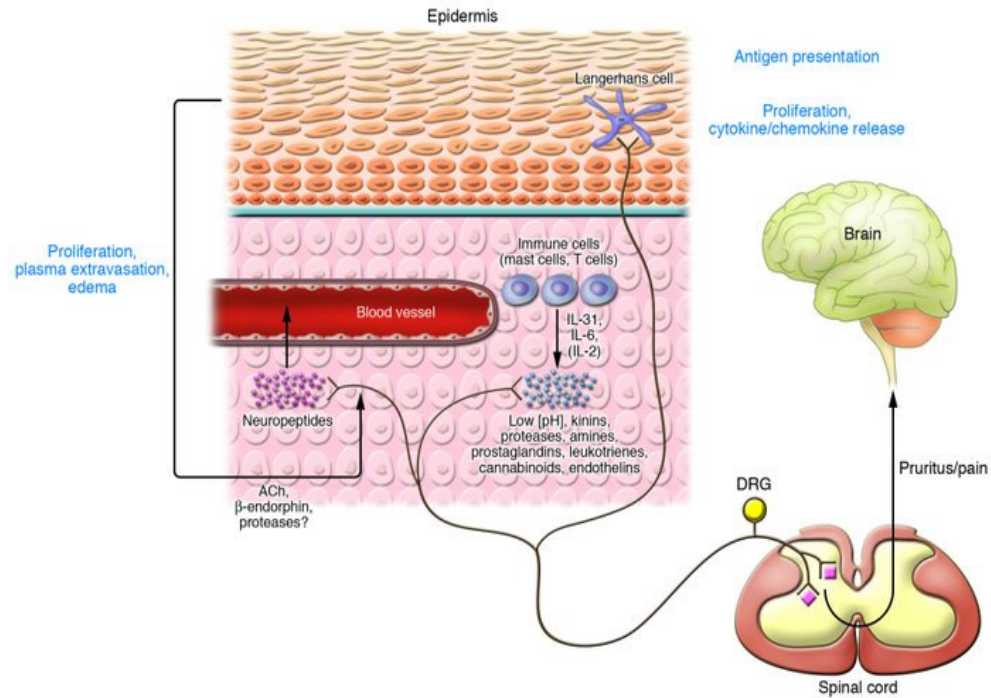


Figure - 1

The primary afferent neurons are located in the dorsal root ganglia of spinal nerves. Axons of neurons that conduct itch are unmyelinated C fibers that penetrate into the epidermis as free nerve endings. The transmitters involved are substance P, neurokinin A and calcitonin gene related peptide (CGRP). Once the C fibers get activated there is release of transmitters into the tissue and is processed along the nerves to the spinal ganglia. From there the itch specific neurons cross over the contralateral side of the spinothalamic tract. With specific projections terminating in the lateral thalamus.

Spinal transmission of itch signals results in release of CGRP and SP with activation of CGRP receptor and neurokinin 1 receptor to transit itch signals centrally.

Neurons from the ventral medial nucleus terminate in the 3a region of the sensorymotor cortex whereas neurons from the medial dorsal nucleus terminate in the anterior cingulate cortex. The urge to scratch is due to the involvement of the motor cortex.

PATHOPHYSIOLOGY OF ITCH IN THE SCALP⁶

The pathophysiology of scalp itching is rarely investigated. The scalp skin has a complex neural structure.

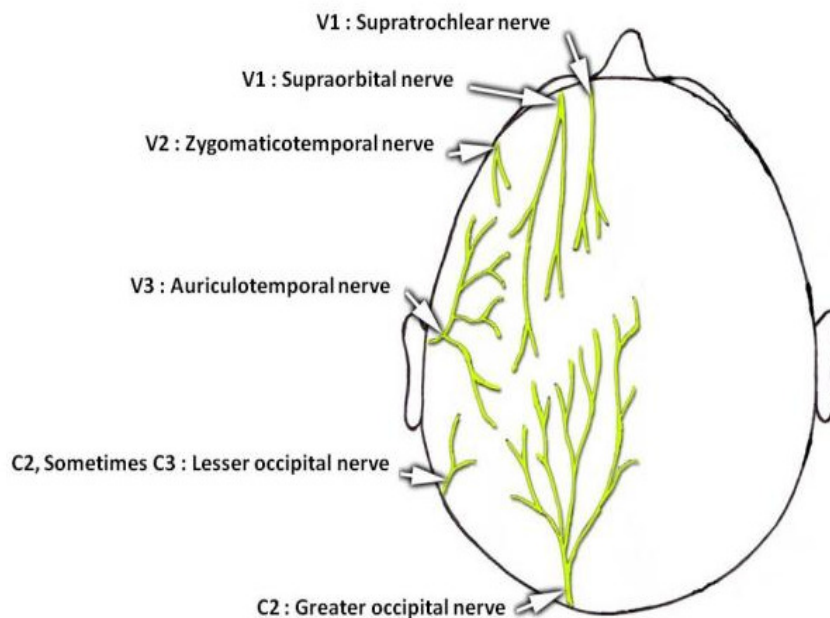


Figure - 2

The hair follicle (HF) is highly innervated with four types of specific nerve endings:⁶

1. Free nerve endings (nociceptors),
2. Lanceolate nerve endings (acceleration detectors),
3. Merkel nerve endings (pressure detectors),
4. Pilo- Ruffini corpuscles (tension detectors) (43 itchy scalp).

Thinly myelinated A-delta fibers or unmyelinated C fibers that emerge from the superficial nerve plexus are the free nerve endings innervating the hair follicle.

Scalp has abundant blood vessels more than in any other body region. Although the scalp is considered extremely itchy in many cutaneous inflammatory diseases experimental studies have shown no differences when compared to itch sensation in other areas of the body.

CUTANEOUS SENSORY RECEPTORS AND MEDIATORS INVOLVED IN ITCHY SCALP

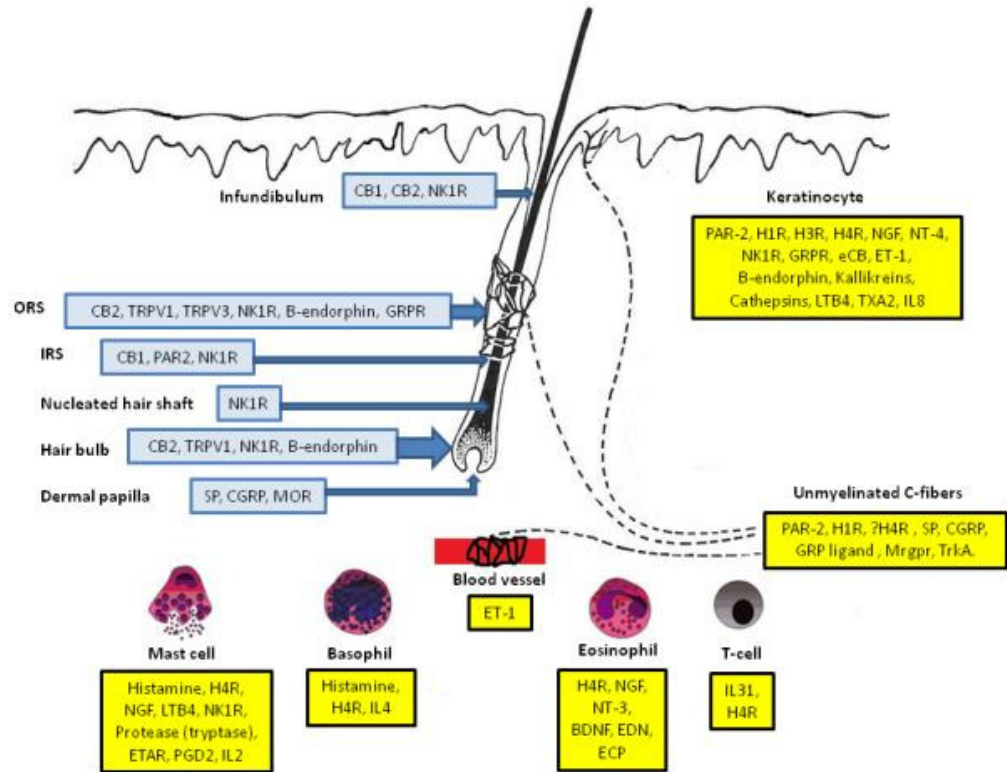


Figure-3

MAST CELLS AND HISTAMINE RECEPTORS

Histamine is the prototype of endogenous itch mediator secreted from mast cells and can induce Pruritus via H1 and H4 receptors on nerve fibers.^{7,8} MC density in scalp skin does not differ significantly from that in forearm skin.⁹

PROTEINASE ACTIVATING RECEPTOR 2 (PAR-2)

It is a G-protein coupled receptor plays major role in mediating chronic pruritus. Cathepsin S which is an endogenous cysteine protease evokes itch and activates PAR-2 and 4. In the skin, PAR-2 is expressed by almost all cell types including keratinocytes, HF, sensory neurons, and MCs.

TRANSIENT RECEPTOR POTENTIAL VANILLOID-TYPE 1 (TRPV1)

It is activated by capsaicin, the key ingredient of hot chilli peppers. When TRPV1 is activated, it causes burning pain, itching and heat sensation, which is suppressed by continuous activation.¹⁰ TRPV1-expressing neurons have multiple intracellular mechanisms that generate or mediate itch.¹¹

OPIOID RECEPTORS

It includes three opioid receptors: Mu (MOR), Delta (DOR) and Kappa (KOR), and the opioid peptides, such as enkephalins, endorphins, dynorphins and endomorphins. μ opioid receptors are up-regulated in atopic dermatitis. Kappa agonists inhibits Pruritus.

CANNABINOID RECEPTORS (CBS)

They are present in the nervous and immune system. In the skin, CB1 and CB2 were observed in cutaneous NFs, MCs, macrophages, epidermal keratinocytes, and the epithelial cells of HFs, sebocytes and eccrine sweat glands.

NEUROKININ RECEPTORS (NKRS)

It is a putative mediator for itching directly and indirectly through MC activation.

ENDOTHELIN (ET)

It evokes pruritus sensation. It is released from endothelium and MCs.^{12,13,14}

CYTOKINES

Certain interleukins (IL) are implicated in the pathogenesis of pruritus. IL-2 is considered a possible pruritogenic mediator and IL-31 a pruritic cytokine.

CAUSES OF SCALP PRURITUS

Pruritus of the scalp can be due to either dermatological or systemic

DERMATOLOGICAL CAUSES

Inflammatory Causes

Seborrheic dermatitis, Psoriasis, xerosis, atopic dermatitis, contact dermatitis, sensitive scalp, lichen planopilaris, urticaria, scars, insect bite, lichen simplex chronicus, lichen nuchae, discoid lupus erythematosus, acne necrotica, folliculitis decalvans.

Infectious Dermatoses

Folliculitis, mycotic, bacterial and viral infections, scabies, pediculosis capitis, cutaneous larva migrans.

Neoplasms

Lymphoma, leukemic infiltrates of the skin.

NEUROPATHIC

Diabetes mellitus, migraine headache, atypical facial neuralgia, scalp dysesthesia, brain and spinal cord injury, Wallenberg syndrome,¹⁵ brain tumors.¹⁶

SYSTEMIC

Chronic renal failure, cholestatic liver disease, Lymphoma- Hodgkins and non hodgkins, dermatomyositis,^{17,18} drug induced Pruritus (e.g dobutamine),¹⁹ Eosinophilic arteritis of the scalp.²⁰

ALLERGIC CONTACT DERMATITIS TO COSMETICS

People use many cosmetic products on a daily basis. Hence allergic contact dermatitis to cosmetics are increasingly observed. The allergens in the cosmetics reach the skin through various different ways

1. By direct application
2. By occasional contact with the allergen
3. Airborne contact
4. Product used by the partner
5. Resulting from a contact with photo-allergen
6. Exposure to sunlight

PATTERNS OF COSMETIC ALLERGY²¹

Contact allergy to cosmetics have specific pattern of dermatitis. It is most often limited to the site of cosmetic application hence diagnosis is clear whereas they also present with dermatitis over other sites. Some of the common patterns of cosmetic allergy are:

1. Facial dermatitis
2. Eyelid dermatitis
3. Neck dermatitis
4. Allergic contact cheilitis
5. Perioral dermatitis
6. Connubial dermatitis

HAIR COSMETICS

A healthy hair is described as a hair that has lusture, is smooth, long, silky and bouncy with good volume and no evidence of balding. To achieve this the hair care industry has given us a plethora of products. Hair cosmetics have become an unavoidable part of life, starting from the shampoos we use.

Almost all of it contains a multiple number of allergens known to cause problems. It is estimated that approximately 800 raw materials are used for making toiletries. Hence it is difficult to find out the exact culprit.

Hair cosmetics can again be wash off and stay on products. Some of the wash off products like shampoos, conditioners etc can also cause scalp pruritus when not washed properly. Stay on products are hair spray, hair dyes, gels etc.

CLASSIFICATION OF HAIR COSMETICS²²

The various components of hair at the molecular level regulate the efficacy of various hair cosmetic products.

Category 1: those that work on the exocuticle (eg- shampoos, conditioners, serums, hair sprays, waxes, gels, mousses)

Category 2: those that work on the cortex or alter the structure of the hair shaft. (e.g- hair colours, bleaching agents, straightening and perming agents)

SHAMPOOS

It is very important to maintain a good scalp and hair hygiene for a healthy hair. In India most of the women have long hair even upto their knees it determines their beauty hence it has to be maintained well. Shampoos are basically formulated for cleansing the hair and the scalp. It was their only function but nowadays various products are being marketed with different properties like, to give shine, volume, to protect colour, for oily scalp, ultra violet protection and so on. Hence people tend to change their shampoos frequently to see a change not realising the fact that it is loaded with allergens.

All the shampoos have some basic ingredients like.²³

1. Detergents
2. Preservatives
3. Fragrances
4. Conditioners
5. Thickeners

6. Opacifiers
7. Special additives
8. Sequestering agents

Shampoos are usually well tolerated but can cause scalp pruritus, eyelid dermatitis, neck dermatitis, facial dermatitis often leading to difficulty in clinical diagnosis.

Fragrances used in shampoos were found to be the most common allergen but it is difficult to find a product free of these allergens. A positive patch test to fragrance is present in approximately 1-4% of the general population and 10% of positive patch test clinic population.^{24,25} This percentage is found to be increasing due to the increase in use of fragrances. ACD to fragrances used in shampoos is less common when compared to leave on products.

Table – 1
TYPES OF SURFACTANT AND ITS PROPERTIES

Type of surfactant	Chemical class	Characteristic of the product
Anionic	Lauryl sulphates, sarcosines, sulfosuccinates, laureth sulphates	Can damage the hair on deep cleansing
Cationic	Long chain amino esters, ammonioesters	Poor lather, poor cleansing, it imparts the softness and manageability
Nonionic	Polyoxyethylene fatty alcohols, polyoxyethylene sorbitol esters	Mild cleanser, imparts manageability
Amphoteric	Imidazolinium derivatives, betaines, sultaines	Mild cleanser, non irritant to the eye, impart manageability.

PRESERVATIVES IN SHAMPOO²⁶

Preservatives in shampoo include sodium benzoate, parabens, 1,3-dimethylol-5, 5-dimethyl (DMDM) hydantoin, tetrasodium EDTA, methylisothiazolinone, and Quaternium-15.

CONDITIONERS

Conditioners are viscous liquid applied to the hair to enhance the feel, appearance, lubricity and general manageability of hair. Shampoos remove sebum along with dirt and other residues from hair and scalp. Sebum like substance was needed to maintain the hair styling hence conditioners came to play.

How conditioners act?^{27,28}

Cationic surfactants of the conditioner carry a positive electric charge which is attracted to the negative charge of the hair. As a result conditioner gets deposited on the hair in areas of weathering. They act best as dispersions rather than solution.

CONDITIONERS CONSIST OF FOLLOWING INGREDIENTS

Cationic surfactant

They are considered as back bone of conditioners. This includes Cetyltrimethylammonium chloride or cetrimonium bromide, stearamidopropyl dimethylamine.

Polymers

Mono and polypeptides like hydrolyze proteins (amino acids), polypeptides derived from collagen and polyvinylpyrrolidone (PVP)

Bodying agents and thickeners

Fatty alcohols (e.g. cetyl alcohol and stearyl alcohol), waxes (e.g. carnauba wax and paraffin wax), or gums (e.g. guar gum) and salt (sodium chloride).

Emollients / oily compounds

These include natural or synthetic oils, but also esters and waxes. Natural oils used in conditioners are, for example, jojoba oil, olive oil, or grape seed oil. The most frequently used synthetic oils are silicone (e.g. dimethicone, dimethiconol, amodimethicone and cyclomethicone) which are even superior to natural oils in terms of film formation, shine and luster. Asian countries have large hair diameters, therefore a higher concentration of silicone is used as compared to that for Caucasian hair (3-5% vs 0.5%).²⁹

Auxiliary emulsifiers

Ethoxylated fatty alcohols (e.g. polysorbate-80 or cetareth-20) which are non-ionic agents seem to be particularly effective at providing emulsion stability if it cannot be achieved by cationic agents alone in a conditioner.

HAIR STYLING PRODUCTS

Hair care industry has provided us with a number of products that helps in changing the texture. Styling products include curling with rollers, ironing, blow drying etc. For this purpose various hair cosmetics are used such as hair sprays, waxes, promades and mousses. These products can be washed off with water or shampoo.

HAIR SPRAYS

Hair sprays were first marketed in the year 1940. Previously women used natural compounds like clays and gums to set their hair. Natural resin materials like shellac were used in the 1st hair spray. Since last 70 years various advancements have been made with the quality of ingredients being used.

How a hair spray works?

These products are in the form of aerosol i.e, they can be sprayed onto the hair to hold the style for a longer time. when sprayed the liquid drops run down the hair shaft once they reach the intersection of two hair follicles it dries and creates an invisible film that bonds the hair together and create stiffness.

The main constituent of hair spray is polymers sometimes called as resins are long chain chemical compounds. It also contains chemical additives and solvents.

Polymers

Polyvinylpyrrolidone is a common polymer used in hair sprays. It does not have a long hold and can be water washed. In addition to this a few products may also contain vinyl acetate which is long lasting hence holds curls better. It is water proof so difficult to shampoo off. Some newer softer hair sprays contain methacrylate.

Solvents

They make up the largest portion of an aerosol hairspray. For example water is a popular solvent due to its low cost but the disadvantage is it takes a long time to dry and it can cause corrosion inside the can. Volatile organic compounds like ethanol belongs to this group but it restricted to use as it can cause air pollution.

Additives

Hair sprays contain a number of chemical additives for example plasticizers are added to modify the effect of polymers. These substances are added to make hair flexible and less brittle. This includes isopropyl myristate, diethyl phthalate and silicones. As corrosion can occur in the spray can anti-corrosion agents like aminomethyl propanol, ammonium hydroxide, cyclohexylamine and borate esters are added to control the resin solubility.

HAIR GELS

These products are mainly useful for individuals who have thinning of hair. They are used for styling and give a gloss to the hair. History says that Egyptian mummies styled their hair using fat based gel. In the 1960s modern hair gel was invented.

The ingredients in hair gel are similar to hair spray, i.e, the primary ingredient is the polymer. Most commonly used are polyvinyl pyrrolidone or vinyl pyrrolidone. A thickener like carbomer which is an acrylic polymer is also used. Apart from these solubilisers, solvents, emollients and colourants are used.

HAIR WAXES

These are wax containing copolymers. The purpose of the product is similar to gel but it is free of alcohol. Some of the ingredients found in hair wax are lanolin, beeswax, emulsifying wax, etc.,

HAIR MOUSSE

It is aerosol foam spray or cream based added to hair for extra volume and shine. The first ingredient in the hair mousse is water which helps to bind the other chemicals together followed by alcohol which helps in dissolving the ingredients. The next ingredient is the polymer or resin which acts as a conditioning agent. It also contains emulsifiers, silicones, vitamins, sunscreens and dyes.

HAIR COLOURS

Greying becomes distressing as it indicates ageing and also early greying of hair in youth. When 20% of hair loses its pigment greying becomes obvious. Hair care industry has provided us with hair colours to hide the same and hence improves the confidence level of a person by making them feel young. The hair colours can be temporary or permanent. They are classified based on the shape of the molecule. Temporary hair colours stay on the hair shaft as it has large molecules. In case of permanent hair dye the molecules are small hence it enables the dye to penetrate the cortex and remains there.

Hair dyes can be classified into 3 main categories:

- A. Vegetable hair dyes
- B. Metallic hair dyes
- C. Synthetic hair dyes
 - a. direct hair dyes
 - b. oxidation hair dyes

VEGETABLE DYES

This group includes henna, chamomile and cinchona. Among them henna is widely used in India. it is obtained from *Lawsonia intermis*. The power or the paste form is obtained from grinding the stem and leaf of the plant which can be made at home. The active ingredient is 2-hydroxy-1,4-naphthoquinone.

Nowadays manufacturers have added PPD to the natural henna for the colour. It is being marketed as kali mehendi. Application of this as a temporary tattoo has become fashionable. That in turn causes contact dermatitis in patients allergic to PPD. Henna by itself has a low allergenic potential but allergic contact dermatitis is mainly due to the additives such as diaminotoluenes and diminobenzenes.³⁰ Pure henna can be applied over the scalp which turns the grey hair red to metallic in colour. This is still a common practise among the Indian women.

METALLIC DYES

This includes silver nitrate, lead salts, copper nickel and cobalt. These products are potentially toxic. They provide wide range of colours to the hair. Since it makes the hair brittle they are used infrequently.

SYNTHETIC DYES

They are again classified as,

- A. Temporary hair dyes
- B. Semi-permanent hair dyes
- C. Demi-permanent hair dyes
- D. Permanent dyes

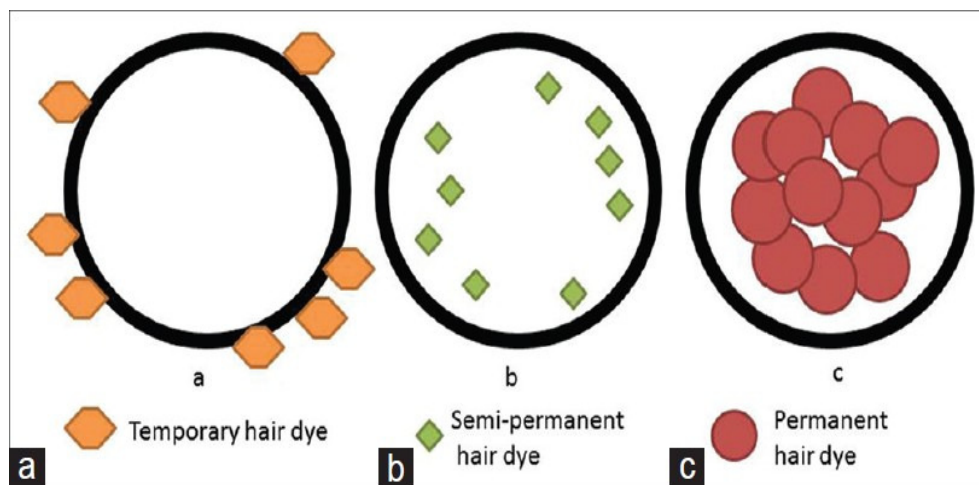


Figure - 4

A. TEMPORARY HAIR DYES:

These are used to brighten the hair shade. Temporary hair dyes have larger molecules so it does not penetrate the hair and gets deposited in the hair shaft. Hence it is easily washed off after shampooing but if the hair is already damaged it can stay for long. Examples of temporary dyes include anthraquinone colours, azo dyes, etc.

B. SEMI-PERMANENT HAIR DYES

Semi-permanent hair dyes can again be oxidative or non-oxidative.

Oxidative Dyes

They contain 2% hydrogen peroxide and low levels of alkalinizing agents like monoethanolamine hence penetration into the hair is more compared to the non-oxidative type.³¹ The colour lasts for around six to eight

washes and are completely removed. Oxidative dyes cover around 50% of the grey hair. These dyes are the common cause of allergic contact dermatitis.

Non-oxidative dyes

These are low molecular weight dyes which enables the product to diffuse into the hair. These include nitrophenylenediamines, nitroaminophenol and anthraquinones. Non-ionic nitro dyes are the most commonly used semipermanent hair dyes.

C. DEMI-PERMANENT HAIR DYES

These are hair colours that contain alkaline agents other than ammonia. This includes ethanolamine and sodium carbonate. It has lower percentage of hydrogen peroxide around 2%.³² Hence damage to the hair shaft is reduced.

D. PERMANENT HAIR DYES

These are the most commonly used hair dyes as it has the highest grey hair covering capacity. Due to the presence of smaller molecular size they penetrate the hair shaft and stays there hence it cannot be easily washed off.

The main ingredient belongs to the group of arylamines, is the combination of para dyes. This includes para-phenylenediamine, para-toluenediamine and para-aminophenol. These primary ingredients have less colour but in the presence of hydrogen peroxide they get oxidized to form colourless quinone-diimines. In the presence of a coupler the polymerized

intermediate reacts to produce the dyes. PPD is a colourless intermediate chemical in the production of dyes and antioxidants.³³

Production of a coloured product is a 3 step process

- I. Oxidation of PPD to quinonediimine which exists in equilibrium with the monoprotonated form.
- II. This attacks the coupler leading to electrophilic aromatic substitution.
- III. Oxidation of the product of previous reaction to form the final dye which gets deposited in the hair as these molecules are large they cannot pass out of the cuticle and remains there until the new hair grows.

Ammonia promotes the bonding of the hair with dye. Nowadays the use of ammonia in hairdyes is markedly reduced. Hence instead of ammonia other alkaline agents like sodium carbonate and ethanolamine are being used.

Based on the colour they produce couplers are in three major classes

- Blue couplers- 1,3-diaminobenzene and its derivatives.
- Red couplers- phenols and naphthols such as 3-methylphenol, 5-amino-2-methylphenol and 1-naphthol.
- Yellow-green couplers- resorcinol, 4-chlororesorcinol and benzodioxoles.³³

EPIDEMIOLOGY OF ALLERGIC CONTACT DERMATITIS TO HAIR DYE

The most important cause of Allergic contact dermatitis to hair dye is due to PPD. It can present as acute, subacute or chronic dermatitis. Among the dermatitis population the prevalence of PPD positivity is found to be 4.3% in Asia, 4% in Europe and 6.2% in North America.^{36,37,38} Recently the prevalence among the Asian population has increased to upto 12% due to increase in the usage.

HAIR BLEACHES OR DECOLOURING AGENTS

These agents are used for hair lightening without adding another colour. Hair bleaches contain hydrogen peroxide, ammonia and persulphate to enhance the efficacy. A mixture of the opens the cuticle and strips the eumelanin from the cortex. This process is capable of bleaching only eumelanin and not pheomelanin. Conditioning following the procedure is necessary as the hair is now damaged.

METHODS OF TESTING COSMETIC ALLERGY

Adverse reactions to cosmetics constitute a small but significant proportion of contact dermatitis cases. This is true in relation to the vast number of cosmetics used. The reaction to cosmetics can present with a classical pattern or just Pruritus. The most common allergens are found to be fragrances but it very difficult to identify as they are considered trade secrets.

Patch test is considered the gold standard for allergen identification however there are other various modes of investigations with less sensitivity.

Photo-patch test

This test is done to detect photocontact dermatitis, the test is considered positive if the test site shows dermatitis on exposure to antigen and sunlight.

Repeated open application test (ROAT)

The suspected cosmetic is applied to a test site, 5cm square area twice daily especially the flexor surface of the forearm. If no reaction occurs after 1 week the product is considered safe. This test can detect allergy due to fragrance and to confirm the clinical significance of weak positive patch test reaction.

Thin-layer rapid use epicutaneous test (TRUE)

TRUE test contains preloaded packs of 23 different allergens or mixes well known to cause contact dermatitis along with negative control. It is a portable and convenient method.

Elimination Test

This test is done when the exact cosmetic causing contact dermatitis is not identified. All the cosmetics are stopped and introduced one by one, if reaction occurs the cosmetic used most recently should be eliminated.

Chemical Analysis

This test is done to identify new unknown allergens or materials containing a suspected allergen.

PATCH TESTING

During the 17th, 18th and the 19th centuries some researchers reproduced contact dermatitis by applying the responsible agents like chemical, plant etc., to the intact skin. Josef Jadassohn, a German dermatologist is universally acknowledged as the father of patch testing. The results of his innovative patch testing was published in the year 1895 and till now it is considered the gold standard for diagnosing allergic contact dermatitis. Initially it was done for patients who had skin intolerance to mercury salts.

In 1931 Sulzberger and wise supported patch testing in cases of eczema and dermatitis. Fisher concluded in his book that ‘properly applied and correctly interpreted patch tests are at present the only scientific proof of allergic contact dermatitis’,³⁹

PATCH TESTING IN THE POST JADASSOHN ERA

Since the discovery of patch testing, much effort has gone into understanding the chemical and toxicologic aspects of test allergens, in standardization and optimization of allergens, vehicles, and concentrations of

patch-test materials. There has been various advances in the procedures of its application, as well as in reading and scoring of test reactions. All this has led to the accurate, reliable and safe test with a high reproducibility of its results.

PURPOSE OF PATCH TESTING

Patch testing is a well-established method of diagnosing contact allergy especially the delayed type of hypersensitivity reaction. To verify the diagnosis of allergic contact dermatitis. Patients with history and clinical picture of the same are re-exposed to the suspected allergens. If the patient does not react to the suspected allergens tested, it is unlikely that he or she will react to the products in ordinary use. It is relatively rare to find out the one substance that definitively accounts for the patient's dermatitis.

When performing patch testing it has to be remembered that the patch test is a biological provocation test and as such the outcome is dependent on multiple factors including the test system and test material, the biological/functional status of the tested person, and the responsible dermatologist.

PATHOPHYSIOLOGY OF ALLERGIC CONTACT DERMATITIS⁴⁰

Allergic contact dermatitis is a type IV hypersensitivity reaction.

The various steps involved in the pathogenesis are:

1. When haptens penetrate the stratum corneum they bind to the dendritic cells.
2. Hapten carrying langerhans cells traverse to the regional lymph nodes through efferent lymphatics.
3. Migrating langerhans cells are located in the para-cortical area of the draining lymphnode where they present the processed antigen to the MHC molecules. MHC class I to CD8+ cells and MHC class II to CD4+ T cells.
4. These proliferated T cells, with the help of efferent lymphatics reach the blood flow.
5. During this process they acquire skin specific homing agents and become memory T cells. Primed T cells diffuse in the skin. At the end of sensitization step there is development of contact sensitization reaction upon challenge with relevant hapten. On subsequent sensitization the haptens diffuse through the epidermis and could be loaded by langerhans cells or other skin cells expressing MHC molecules such as keratinocytes and dendritic cells which then activate specific T-cells.
6. Activation of CD8+ T cells initiates the inflammatory process through keratinocyte apoptosis and cytokine production.

7. This is responsible for recruitment of leukocytes from the blood to the skin resulting in development of skin lesions.

IDEAL CANDIDATE FOR PATCH TESTING

Allergic contact dermatitis can occur at any age hence even patch testing can be done at any age. It is indicated in patients with underlying suspected allergic contact dermatitis in whom the dermatitis can be acute, subacute, chronic, pruritic or lichenoid dermatitis. Individuals with Atopic dermatitis have increased sensitivity to contact dermatitis when compared to the nonatopic individuals. Atopic individuals have chronic and daily exposure of allergens in their creams, lotions and topicals which leads to greater cumulative skin exposure. Hence patch testing should be done in patients who do not respond to topical treatment. History and physical examination alone is not adequate as history can diagnose only 29-54% of allergic contact dermatitis.(1-practical guide PT) Hence patch testing is essential to confirm the diagnosis.

WHEN TO AVOID PATCH TEST

Patch test has to be avoided in:

- I. Patients with acute generalized dermatitis or erythroderma where lesions are present over the back so patch test cannot be done until the dermatitis subsides.
- II. Patients who are on immunosuppressive agents like systemic steroids, cyclosporine, cyclophosphamide etc., as it can mask the inflammation.

- III. Topical steroids, calcineurin inhibitors, applied to the patch test site may also reduce the patch test responses.

PATCH TEST ALLERGENS

Patch test series are available from the Chemotechnique diagnostics, AllergEAZE, Trolab Hermal and many others. It is impossible to check the thousands of allergens currently known to cause allergy. A small number of allergens most commonly known to cause allergy are grouped under the standard series. This standardization of allergens is done by the experienced members of the International Contact Dermatitis Research Group (ICDRG). Apart from the standard series there are many others like cosmetic series, dental series, steroid series, shoe series and many others. These are tested according to the specific indication.

PATCH TEST VEHICLES

Each allergen has its own optimal vehicle. White petrolatum is the most widely used vehicle. It gives good occlusion, keeps the allergen stable and its inexpensive. The disadvantage is it can retain the allergen and cause skin irritation. Liquid vehicles like water and solvents like acetone, ethanol are recommended but it has its own drawbacks. Liquid vehicles are mainly used in testing patients own products. Solvents may evaporate which does not favour exact dosing.

PATCH TEST CHAMBERS

The basic requirements for a patch test chamber are an inert material applied to a hypoallergenic tape particularly scanpor tape. The tape is provided for good occlusion and fixation to the skin. In recent years aluminium Finn chambers are being used. The size of it varies from 8mm to 12mm. They are available in a strip of five and ten.

CONCENTRATION OF ALLERGENS

Concentration varies for each allergen. Excessive concentration can lead to false positive reactions, irritant reactions and low concentration can lead to false negative reactions. Hence an ideal concentration must be used.

STORAGE OF ALLERGENS

The allergens should be stored in a cool (refrigerator) and dark place at 4 degree C. Homogeneity of allergens may be lost if not stored properly. When diluted in liquids it should be kept in dark bottles. Commercial preparations are labelled with expiry date.

PATCH TESTING METHODOLOGY

Upper back is the preferred site for patch testing due to the large surface area. Other acceptable site is the arm. If tested in other areas false negative results can be obtained. The area tested must be free of hair, moisturizers and

other oily substances as it is difficult to get adequate skin contact. If oil is present it can be gently removed by wiping with ethanol or other solvents.

During application patients are asked to sit erect and patches are applied to the mid-back area 2.5cm laterally as the patches may be detached. Test strip should be applied from below upwards with mild pressure followed by firm strokes to promote uniform distribution of the allergen. The patches are reinforced with an additional tape.

INSTRUCTIONS TO THE PATIENT

1. Patch should be left in place for two nights and three days.
2. To avoid taking bath.
3. Do not wash the area.
4. Do not expose the back to sunlight.
5. Avoid vigorous exercise, swimming and sports during testing.
6. Avoid tight underclothes.
7. Avoid scratching the patch test site, in case of severe itching report.

PATCH TEST READING

Patches are placed for 48hrs unless there is severe reaction and significant discomfort. The reading is taken 20-30 min after removal of patches to allow erythema from the occluding pressure. Lighting should be good while taking the reading. The site should be marked with indelible ink or stratum corneum stains before taking the reading for proper identification and to avoid

confusion. The second reading is taken at 72hrs. Some authors have suggested reading at 96hrs. The second reading is necessary because a few percentage of relevant allergens that was negative at 48hrs could become positive at 72hrs and vice versa.

PATCH TEST REACTION SCORING

The most common and agreed method of patch test reading was proposed by ICDRG in the year 1970. It is a subjective method based on the inspection and palpation of the test area.

PATCH TEST RELEVANCE

It does not end with the final reading of the test and identification of the allergen. The clinician must correlate whether such allergen is responsible for the dermatitis either as a primary cause or an aggravating factor. This is the crucial phase of the procedure.

The currently used classification of clinical relevance is:

1. Relevance to present dermatitis
 - a. Primary cause
 - b. Aggravating factor
2. Relevance to a preceding bout of dermatitis
 - a. Primary cause
 - b. Aggravating factor
3. Not relevant
4. Unknown or “unexplained positive”

It is impossible to provide rules for relevance as it is based on the blend of knowledge and experience of the clinician. The absence of patch test results does not prove the absence of allergy it only means that the patient is negative to the more common and well established sensitizers.

VARIABILITY IN PATCH TEST

Variable results in patch test is due to various factors.

Materials

Type of patch test system used, sources of patch test allergen, vehicle and concentration of allergens.

Methodology and technique reasons

Criteria used for patient selection, application of the test, amount of allergen applied, integrity of the test and interpretation of responses.

Biological reasons

Regional variation in skin absorption and responsiveness, intercurrent factors, skin hyporeactivity and hyperreactivity.

CAUSES OF IRRITANT PATCH TEST REACTION⁴²

Irritant patch test reactions are due to:

- i. Hyperirritability of the skin.
- ii. Irritating concentration of the test substance.
- iii. A combination of both.

REASONS FOR FALSE NEGATIVE REACTIONS⁴³

Various causes of false negative reactions are:

1. Low concentration of the test substance.
2. Wrong carrier vehicle resulting in inadequate penetration.
3. Failure to perform delayed reading
4. Wet or loosened patches.
5. Duration of contact is too weak.
6. Failure to perform delayed readings.
7. Patches applied at wrong site.
8. Allergen degradation.
9. Use of immunosuppressives.
10. UV radiation at site.

REASONS FOR FALSE-POSITIVE REACTIONS

The following are reasons for false positivity in patch test.

1. Higher concentration of test substance.
2. Excessive amount of allergen.
3. Uneven dispersion of allergen.
4. Recent active dermatitis at the patch test site.
5. Active dermatitis at the distant site.
6. Angry black syndrome.
7. Pressure reaction from the chamber.

8. Adverse reaction from the vehicle.
9. Irritant reaction due to adhesive tapes.
10. Cross reacting and co-sensitizing substances are tested in too close proximity.

TESTING OF PATIENTS OWN PRODUCTS

Safety assessment of a cosmetic product depends upon how it is used. High concentration of the product can result in irritant reaction or false positive reaction. Patch testing of the patient's own sample is essential because all the ingredients in the product is not included in the series. It contains only the common allergens. In case of shampoos and conditioners it is diluted in a ratio of 1:10.

ADVERSE PATCH TEST REACTIONS

- Active sensitization
- Edge effect
- “Ectopic” Flare of Dermatitis
- Persistence of a Positive Patch Test Reaction
- Koebner phenomenon – patient having psoriasis or lichen planus
- Alteration in pigmentation- occur in darkly pigmented persons.
- Anaphylaxis reaction can occur within 30 minutes after application of topical antibiotics such as penicillin, gentamycin, neomycin and bacitracin

- Pustular Patch Test Reactions
- Bacterial and viral infections⁴⁴
- Pruritus
- Pressure effect- more common in persons who have a tendency to develop dermographism.
- Leakage of material on to the clothing, especially dyes
- Folliculitis
- Localized flare of dermatitis and other skin disorders
- Generalised flare of dermatitis
- Flare of dermatitis at previous contact site
- Necrosis, scarring, and keloids⁴⁵ - usually associated with very strong patch test reaction.
- Milia⁴⁶

ALLERGENS - COSMETIC SERIES

1. Control

2. Hydroabietyl alcohol

It is an organic alcohol derived from wood rosin. It is a colourless balsamic resin used in styling gel, lotion, mascara, as adhesives. This product is banned in EU.

3. Amerchol L- 101

It is obtained by the hydrolysis of lanolin and lanolin is a natural product obtained from the sebaceous glands of sheep. Amerchol is a trade name of product containing lanolin alcohol. It is used in hair products, moisturizers, lip sticks also present in non cosmetic products like furniture polish, leather, paper inks, textiles, cutting oil etc., according to the NACDG data the prevalence of patch test positivity to lanolin is 2.2%.⁴⁷

4. Benzyl alcohol

Other term used to describe benzyl alcohol are benzene methanol, phenyl methanol and phenyl carbanol. It is a preservative and has antibacterial properties mainly against gram positive bacteria. Some of its additional properties are its local anaesthetic action and fragrance properties. Hence used widely in perfumes and increasingly in hair dyes. The use of benzyl alcohol results in deeper shades in dye concentrations. Curry and Warshaw reported a patient with ACD who had 10 year history of using 7 skin care products with

benzyl alcohol⁴⁸ Benzyl alcohol has also been reported to cause non-immunologic contact urticaria.

5. Benzyl Salicylate

It is one of the common fragrance ingredients, used in shampoos, hair dyes, deodorants, soaps, also in non cosmetic products like house hold cleaners and detergents. It is a colourless liquid with very faint, slightly balsamic odour.

6. 2-bromo 2- nitropropane-1,3-diol

It is also known as bronopol, a preservative and anti bacterial agent mainly against gram negative bacteria. Commonly used in cosmetics, hair conditioners, cleansers. Concentration in these preparations is less than 0.1%. Peters et al reported that the incidence of positive patch test with bronopol 0.5 or 0.25% was 12.5% in their study.⁴⁹ ACD to bronopol is more common in certain occupations such as hair stylists, janitorial services, farmers, painters, and printers.

7. 2-tert-butyl-1-4-methoxyphenol

Also called as butylated hydroxyanisole (BHA). It is an antioxidant used in cosmetics, topical medicaments, petroleum, mineral oil etc. it has broad spectrum anti bacterial action. It is most commonly used than BHT. Prevalence of reaction to BHA is low.⁵⁰

8. Butylated hydroxytoluene (BHT)

Common antioxidant and it also has anti bacterial action particularly against corynebacterium species. The prevalence of patch test positivity is

0.5% among 900 patients in a study by Fransway.⁵¹ Most patients allergic to BHT are also allergic to BHA.

9. Cetyl Alcohol

It is an emulsifier and stabilizer also may be considered preservatives. It is often used together with stearyl alcohol under the name cetostearyl alcohol. Allergic reactions to both the agents are very rare. These are used commonly in hair sprays.

10. Chloracetamide

It is a water soluble preservative useful against yeasts and fungi. It is present in cosmetic products, paints, adhesives etc,. Because it is used at a low frequency prevalence of allergy to this product is low. In a report from the Swiss contact dermatitis research group the prevalence of allergy to CAA is 1.5% among 2,295 patients studied.⁵²

11. Chloroxylonol (PCMX)

Also known as parachlorometaxylenol (PCMX) is a halogenated phenol. It's a preservative and a disinfectant. Its activity is against both gram positive and gram negative bacteria. They are more commonly used in industrial products however they are also used in shampoos, skin cleanser, deoderants. It occasionally causes ACD.

12. Gallate Mix

Gallate mix is a mixture containing Propyl gallate, Dodecyl gallate and Octyl gallate. These compounds are antioxidant preservatives. Chemically,

gallates are alkyl esters of trihydroxybenzoic acid. This product is used since 1947 in cosmetics, pharmaceuticals, and food industry for preventing the oxidation of unsaturated fat. In cosmetics gallates are mainly present in waxy and oily products like lip sticks, creams etc. the most commonly used gallate in the industry is propyl gallate. Hence sensitization due to gallates could mainly be due to propyl gallate. However Hausen and Beyer have reported dodecyl gallate to be more sensitive.⁵³ The ideal patch-test concentrations for gallates are propyl gallate at 1%, octyl gallate at 0.25%, and dodecyl gallate at 0.25%, all diluted in a petrolatum or olive oil vehicle.^{54,55} Cross reactivity between gallates can occur because of the similarity of base compounds. Hence if patient tests positive for one gallate all other gallates should be avoided. But if tested with all three and allergic to one then the particular allergen should be avoided.⁵⁶

13. Geranium oil bourbon

It is extracted from the plant *Pelargonium odorantissimum*. This plant is known for its fragrance in various products. Oil content of the flower is less than that of the leaf. The oil is colourless with a watery viscosity. Some of the other therapeutic properties of geranium oil are astringent, diuretic, haemostatic etc., it is mainly used in cosmetics, ointments, dusting powder.

14. Benzophenone-3

Its widely used in sunscreens, they are also found in many other skin and hair care products. It has a property to inhibit degradation of colours hence

added to paints and varnishes. According to the NACDG data positive patch test reaction was 0.7% among 5144 patients.⁵⁷

15. Drometrizole

It is a UV absorbing agent in topical products. It is a broad spectrum UV absorber used in sunscreen cosmetics such as creams, lotions, lipsticks, sun oils and other sunscreen, sunblock or suntan lotions. Used in noncoloring hair care and nail care products at low concentrations.

16. Imidazolidinyl Urea

It is also known as germall 115. It is a formaldehyde releasing preservative most commonly used in cosmetic preparations after paraben. It is nontoxic, non irritating hence compatible with most of the cosmetic ingredients. It also has anti bacterial action effective against both gram positive and negative bacteria. In a study conducted by fisher, among 30 patients allergic to formaldehyde only 1 reacted to IU and 9 reacted to Q-15.⁵⁸

17. Isopropyl Myristate

It is an emulsifier used in various cosmetics. Contact allergy to this allergen is very rare. German investigators have reported many irritant reactions with 20% IM when compared to 10%. Out of 12,000 patients positivity was seen only in 16 patients.⁵⁹

18. Jasmine Absolute

It is a fragrance with unique floral aroma of its own. It harmonizes well with all other essences. It is a pure form of jasmine essential oil. Organic solvent

extraction method is the method used to to extract the jasmine absolute. There are 3 varieties of jasmine that are available and any variety can be used. It is used in hair and beauty products as a sensual perfume.

19. Lavender absolute

It is a dark-green liquid, which smells sweeter and less floral than the essential oil. Absolutes are fragrant oils that are extracted from flowers and plant materials using the solvent method of extraction. It has antiseptic, antibacterial and healing properties.

20. Musk Mix

Musk mix is a mixture made up of Musk xylene, Musk ketone and Musk moskene. These chemicals are synthetic nitro musk compounds. They are used as fragrances and fixatives in cosmetics, after shave lotions and perfumes. A case of ACD to musk moskene in cosmetic cream has been reported.

21. Phenyl Salicylate

It is a chemical substance created by heating salicylic acid with phenol. It acts as an analgesic, antibacterial and UV filtering agent (preventing it from entering the cosmetic container). In cosmetics they are found in suntan oil, hair sprays, creams, softners.

22. Polysorbate 80

Also known as Polyoxyethylene-sorbitan-20-monooleate or tween 80. It is a synthetic compound, which is water soluble yellow fluid. It is used as an emulsifier and surfactant in cosmetic creams, lotions, shampoos, foundation etc., also used in food and pharmaceutical preparations. The cosmetic grade of polysorbate 80 has more impurities than the food grade.⁶⁰ There are reports of polysorbate 80 causing anaphylactoid reactions.⁶¹

23. Rosadamascena Extract

Rosadamascena is a most important species of rosacea family. It has anti oxidant, fragrance, antitussive, hypnotic, antidiabetic, and relaxant effect properties. Used in various cosmetics mainly for the fragrance.

24. Sorbic acid

It is known chemically as 2,4-hexadienoic acid and 2-propenyl-acrylic acid. It is obtained from berries of mountain ash, also present in cranberries, strawberries and currants. It is a white, colourless powder with a faint acid taste. It is used in cosmetics, topical products and pharmaceutical agents. Salt form of sorbic acid is potassium sorbate, is soluble in water, alcohol and propylene glycol. It has an excellent fungistatic agent. Sorbic acid 0.2% is an antimicrobial agent of choice in cosmetics containing fatty acids and polyoxyethylene esters. Patch test prevalence rate of sorbic acid in US is less than 1%. inhalation of pure sorbic acid should be considered a medical emergency.

25. Sorbitan Oleate

Sorbitan Oleate is the monoester of oleic acid and hexitol anhydrides derived from sorbitol which is often used as a humectants. Sorbitan is an anhydride form of sorbitol. It is used in various formulations in cosmetic industry as a emulsifier. Found in cosmetics like skin care products, moisturizers, eye makeup and in other pharmaceutical ointments and creams. It is generally considered mild skin irritants.

26. Sorbitan Sesquioleate

It is an emulsifier used in a number of cosmetic products. It is added to fragrance mix allergens to enhance stability. Contact dermatitis due to this allergen is rare but occasional cases of fragrance allergy is due to this additive in the mix.⁶²

27. Stearyl Alcohol

It is a fatty alcohol, hence insoluble in water. It is widely used for hair coating in shampoos and conditioners. It has properties of an emollient, emulsifier and thickener. It is also used as an ingredient in cosmetics, perfumes and in lubricants.

28. t-butyl hydroquinone

It is an organic compound derived from hydroquinone. It is highly effective as a preservative and antioxidant. They are used in various cosmetic preparations like lipsticks, eye shadow, hair oils, perfumes and skin care preparations at concentrations of 0.1% to 1.0%. TBHQ in hair dye causing contact dermatitis has been reported.⁶³

29. Thimerosal

It is a mercuric derivative of thiosalicylic acid. It is a most common preservative used in cosmetics, contact lens solution and vaccines. Most of the sensitization cases are due to its presence in vaccines. Prevalence of patch test positivity to thimerosal ranges from 1.6 to 37.6 in various studies.^{64,65,66} NACDG has stopped testing this allergen since 2003 due to the frequency of non relevant reactions.⁵⁷ However, FDA has banned the use of mercury products in cosmetics.

30. Triclosan

Also known as 2,4,6-trichloro-1,3-bis(4-chlorophenyl)benzene (Irgasan DP-300), is an antibacterial agent and preservative. It is mainly present in shampoos, soaps and deodorants. Allergic reaction to triclosan is rare and the reported prevalence rate is less than 0.5%..⁶⁸

31. Triethanolamine

It is also known as trolamine, produced from the reaction of ethylene oxide with aqueous ammonia. It acts as a PH balancer, excipient (a substance

that gives its topical agent the proper consistency). Frequently used in shampoos, skin lotions, shaving lotion and occasionally pharmaceutical preparations. There are reports of ACD due to its sensitization.⁶⁸ In products intended for prolonged contact with the skin, the concentration of Triethanolamine should not exceed 5%.

32. Vanillin

It is a phenolic aldehyde and it's the primary component of vanilla bean. Synthetic vanillin can be produced from pine tree sap, wood pulp, sugar and coal tar. They are used in cosmetic industry for the fragrance. For patch test purpose 10% vanillin is used.

33. Oleamidopropyl Dimethylamine

One of the rare causes of ACD. It is a surfactant and emulsifier used in cosmetics, baby lotions and body lotion. According to some data OPD has the potency to produce irritant patch test reactions.⁶⁹ Hence patch testing should be done with 0.1% of aq OPD. In a study done in Netherland ACD to OPD was 11% among 119 patients.⁷⁰

34. Cetrimonium Bromide

It is also known as cetyltrimethylammonium bromide, hexadecyltrimethylammonium bromide is a cationic surfactant. It is one of the components of topical antiseptic cetrimide which is effective against bacteria and fungi. It is widely used in hair conditioning products. It is also

used in shampoos, cosmetics and hair products. Due to its high cost they are used only in selected products.

35. Jasmine Synthetic

These are fragrances used in shampoos, conditioners, hair oil and other cosmetics.

36. Methenamine

It is also known as Hexamethylenetetramine is a heterocyclic organic compound. It is a white crystalline compound highly soluble in water. It is an antimicrobial preservative. It is used in cosmetic products as it works by forming formaldehyde. Used in cosmetics, shampoos, conditioners and eye makeup preparations. Also used in medications for urinary tract infections as insecticide and pesticide.

37. Chlorhexidine

It is used as a disinfectant and bactericide active against both gram positive and gram negative bacteria. It is occasionally used as a preservative in topical preparations. Mainly used in cosmetics and pharmaceutical preparations. Patch testing is done with 0.5% aqueous. Allergy to chlorhexidine can cause contact urticaria and anaphylaxis.⁷²

38. Phenyl Mercuric Acetate

It is an organomercuric compound, which is a preservative, fungicide and herbicide. Found in cosmetics, eye makeup products, eye drops, also found in skin lightening soaps and creams. In sensitized persons patch test can be done at a concentration of 0.01% to 0.16% in petrolatum.

39. Cocamidopropyl Betaine

It was introduced in the year 1970 as organic compounds derived from coconut oil and dimethylaminopropylamine.⁷³ It is a surfactant with low irritancy potential. Used in shampoos, bath gels, liquid detergents and pet shampoos as viscosity builder and foam booster. Most of the cases of ACD to CAPB have been caused by shampoos.^{74,75} Patch test should be performed with a concentration of 5%.

40. Diazolidinyl Urea

It is the newest among the formaldehyde releasing preservative introduced in 1982 as germall II. It is superior to IU but for the antifungal efficacy it has to be combined with other agents. They are commonly used in hair gel, shampoo, cosmetic creams and lotion. The prevalence of positive reactions to DiU is 3.5% according to a data compiled by NACDG.⁵⁷

41. Ethylenediamine Dihydrochloride

Ethylenediamine dihydrochloride is a colourless liquid. It is used as a preservative, emulsifier and stabilizer used in various cosmetics and dyes. It is also a component of insecticides and synthetic waxes. It has fungicidal action in water based products.

42. Quaternium-15

It is a preservative most commonly used in topical preparation, cleanser, lotion, hair care and industrial products. It is colourless odourless and highly soluble in water. Most of the patients who are allergic to Q-15 are also allergic to formaldehyde. In a report published by NACDG between 2002 and 2004, Q-15 was the 5th most common allergen.⁵⁷ It is more prevalent among the health care workers, hair stylists and machine tool workers.⁷⁶

43. Propylene Glycol

It is a dihydric alcohol which is highly hygroscopic. It is widely used in cosmetics, various hand and body lotion as a preservative. It has antibacterial and antifungal properties of above 25%. The amount of PG is as high as 70% in certain preparations. PG in high concentration is somewhat effective for the treatment of tinea versicolor and seborrheic dermatitis.⁶⁷ Various authors have done patch testing with 20% PG with minimal positivity and concluded that undiluted PG is a skin irritant.^{77,78} In contrast testing with low concentrations

of PG (less than 10%) will probably miss true positive reactions. Claveie et.al in their study stated that patch test was negative with 5% PG but positive with 10 or 20%.

44. Methylisothiozolinone / Methylisothiazolinone

The trade names are kathon CG (mixture of MCI and MI in a 3:1 ratio) and euxyl K100 among others. It is a preservative known for its efficacy. Used in cosmetics, lotions, moisturizers, sanitary wipes, shampoos, and sunscreens. Since the prevalence of patch test positivity was high in few reports.^{79,80} The use of it was limited only to the rinse off products only at concentration of 15 ppm or less.

45. Para-phenylenediamine

PPD is an aromatic amine compound. It is white to light purple in colour, on exposure to air it oxidizes first to red, then brown and finally black. It is a primary ingredient in hair dye used at a maximum concentration of 4%. Short term exposure to high levels of PPD can cause severe dermatitis, eye irritation and also systemic complications like asthma, renal failure, gastritis, tremors, convulsions and coma in humans. Apart from its use in hair dye its also used in textile dyes, photographic development agents, also as an antioxidant in rubber compounds.

1% PPD in petrolatum is used in a standard closed patch test. Patients sensitive to PPD may develop possible cross reactions with local anesthetics like procaine and benzocaine, sulfonamides, para-amonobenzoic acid

sunscreens. Several patients have been reported to have immediate hypersensitivity reaction to PPD.⁸¹

MATERIALS AND METHODS

STUDY DESIGN

It is a hospital based Open label prospective study.

STUDY POPULATION

All patients aged 15-70 yrs male or female attending dermatology out patient department with complaints of scalp pruritus. A total of 25 patients with scalp pruritus with or without other dermatosis due to various causes were selected.

STUDY PERIOD

After obtaining clearance from the ethical committee this study was done during a period of 18 months. Written informed consent was taken from all patients involved in our study.

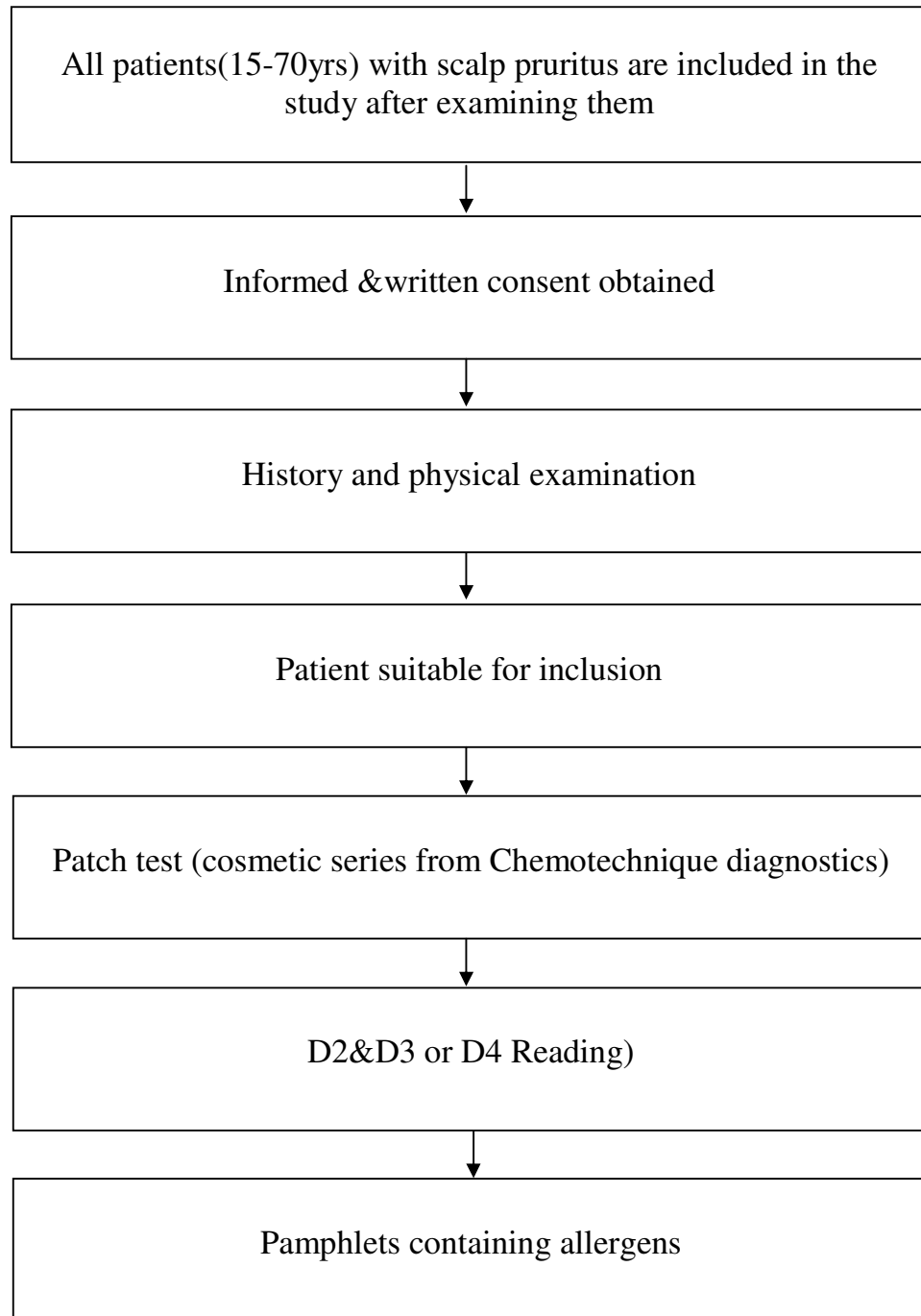
INCLUSION CRITERIA

All patients with history of scalp pruritus with or without other dermatosis of the scalp were included in the study.

EXCLUSION CRITERIA

1. Patients on systemic steroids
2. Patients on oral immunosuppressives
3. Patients having lesions in back due to other conditions

METHODS



INTERPRETATION OF THE RESULTS

Patch test results were recorded according to International Contact Dermatitis Research Group grading

Table - 2

ICDRG CRITERIA

Score	Reaction
– (0)	Negative
? +	Doubtful reaction; faint erythema only
+	Weak positive reaction; palpable erythema, infiltration, possibly papules
++	Strong positive reaction; erythema, infiltration, papules, vesicles
+++	Extreme positive reaction; intense erythema and infiltration and coalescing vesicles
IR	Irritant reaction of different types
NT	Not tested

Table - 3
COSMETIC SERIES

S.No.	ANTIGEN	%
01	Control	100
02	Hydroabietyl Alcohol	10
03	Amerchol L-101	50
04	Benzyl Alcohol	10
05	Benzyl Salicylate	10
06	2-Bromo 2-Nitropropane-1, 3-Diol	0.25
07	2-Tert-Butyl-4-Methoxyphenol(BHA)	2
08	BHT	2
09	Cetyl Alcohol	5
10	Chloroacetamide	0.2
11	Chloroxylenol (PCMX)	0.5
12	Gallate Mix	1.5
13	Geranium Oil Bourbon	2
14	Benzophenone-3	10
15	Drometrizole	1
16	Imidazolidinyl Urea	2
17	Isopropyl myristate	20
18	Jasmine Absolute	2
19	Lavender Absolute	2
20	Musk mix	3
21	Phenyl Salicylate	1

22	Polysorbate 80	5
23	Rosadamascena Extract	2
24	Sorbic Acid	2
25	Sorbitanoleate	5
26	Sorbitan Sesquioleate	20
27	Stearyl alcohol	30
28	t-Butyl hydroquinone	1
29	Thimerosal	0.1
30	Triclosan	2
31	Triethanolamine	2
32	Vanillin	10
33	Oleamidopropyl Dimethylamine	0.1
34	Cetrimonium Bromide	0.5
35	Jasmine synthetic	2
36	Methenamine	2
37	Chlorhexidine digluconate	0.5
38	Phenyl Mercuric Acetate	0.01
39	Cocamidopropyl Betaine	1
40	Diazolidinyl Urea	2
41	Ethylenediamine Dihydrochloride	1
42	Quaternium-15	1
43	Propylene glycol	5
44	Methylisothiazolinone + Methylchloroisothiazolinone	0.02
45	PPD	

RESULTS

Table -4

AGE AND SEX DISTRIBUTION

Age in years	Sex		Total	Percentage
	Male	Female		
10 - 20	0	0	0	0
21-30	5	0	5	25%
31-40	0	2	2	10%
41-50	0	4	4	20%
51-60	3	4	7	35%
61-70	1	1	2	10%

- Among 20 patients included in the study 9 were male and 11 were female.
- Scalp pruritus was more in the elderly age group of 51-60 years.

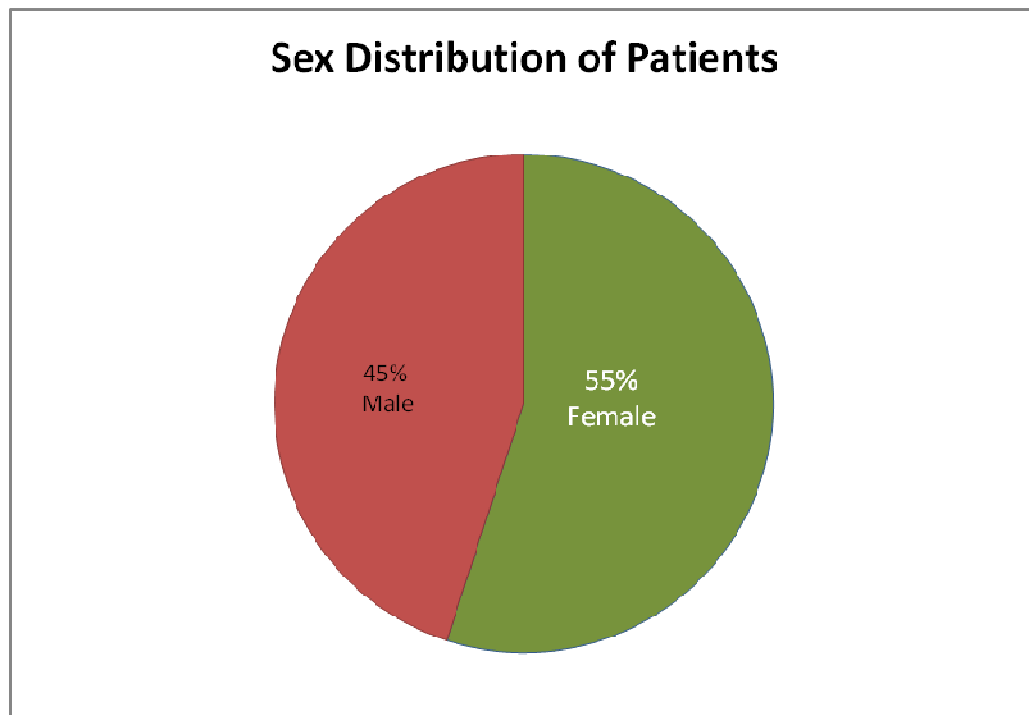


Figure -5

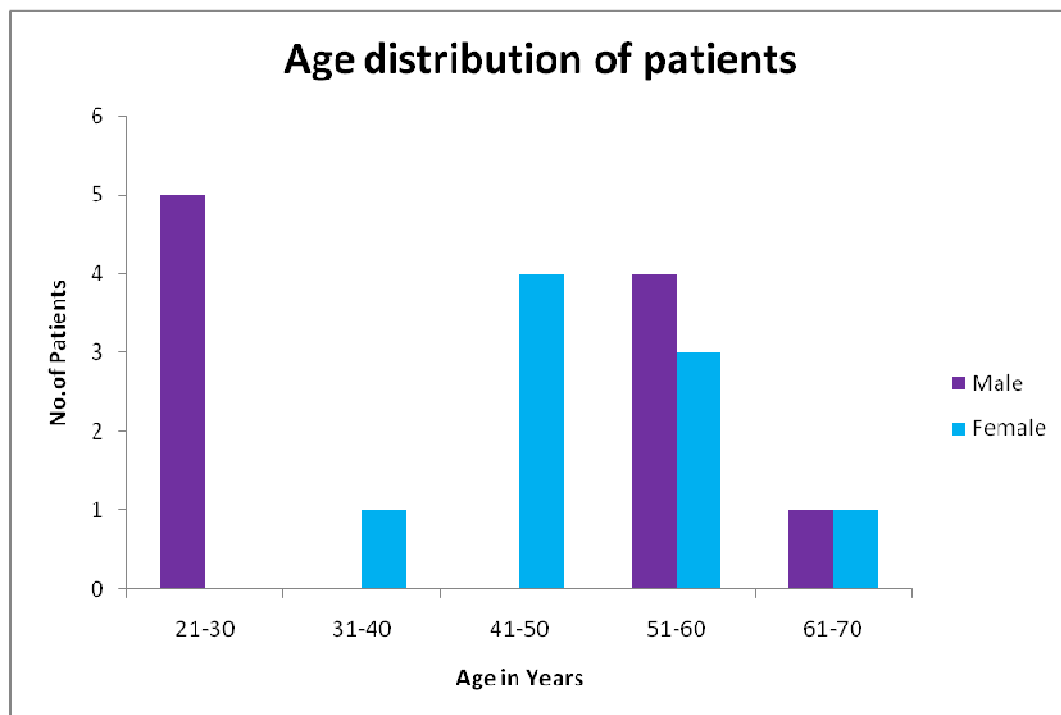


Figure -6

Table - 5

DISTRIBUTION OF DURATION OF SCALP PRURITUS

Duration of itching in months	Number of patients	%
0-3	11	55%
3-6	3	15%
6-9	2	10%
9-12	3	15%
>12	1	5%

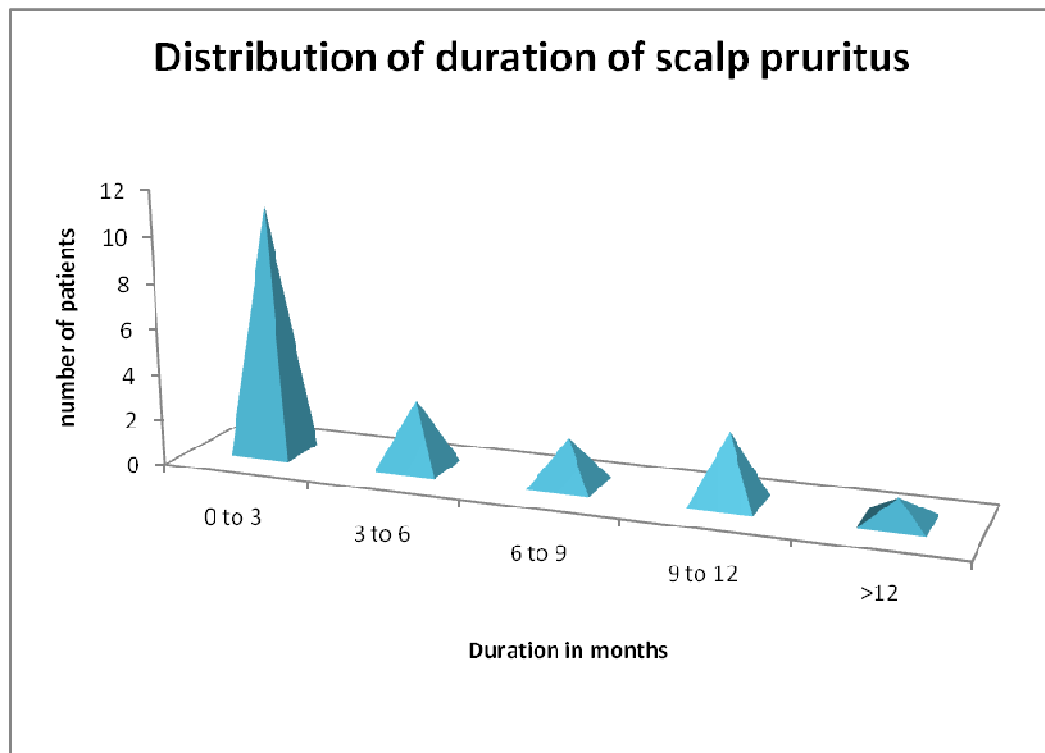


Figure - 7

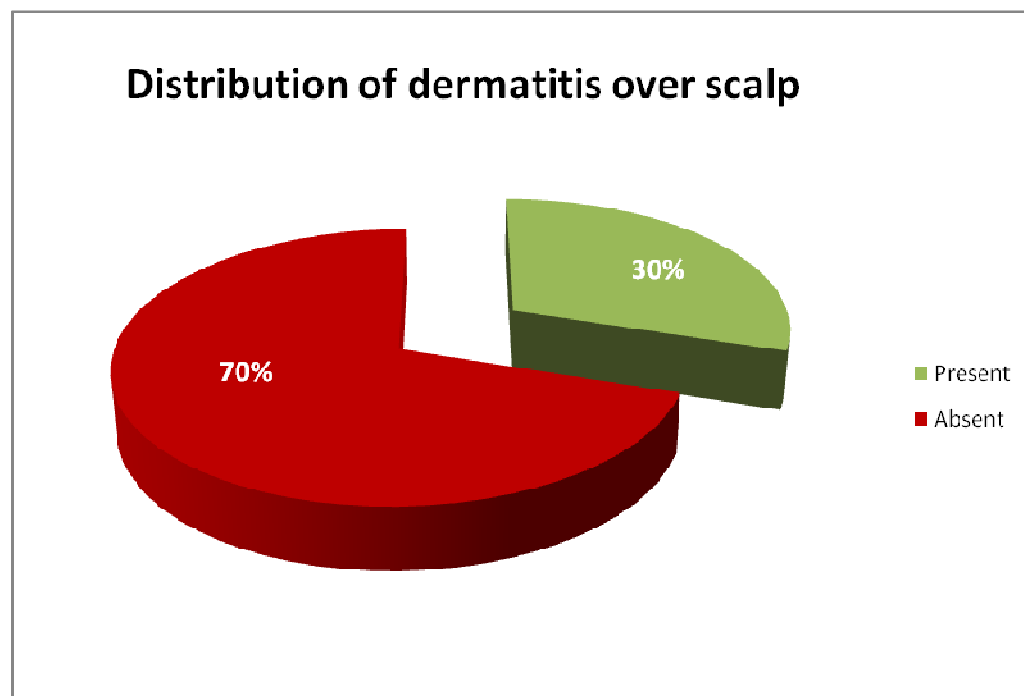


Figure - 8

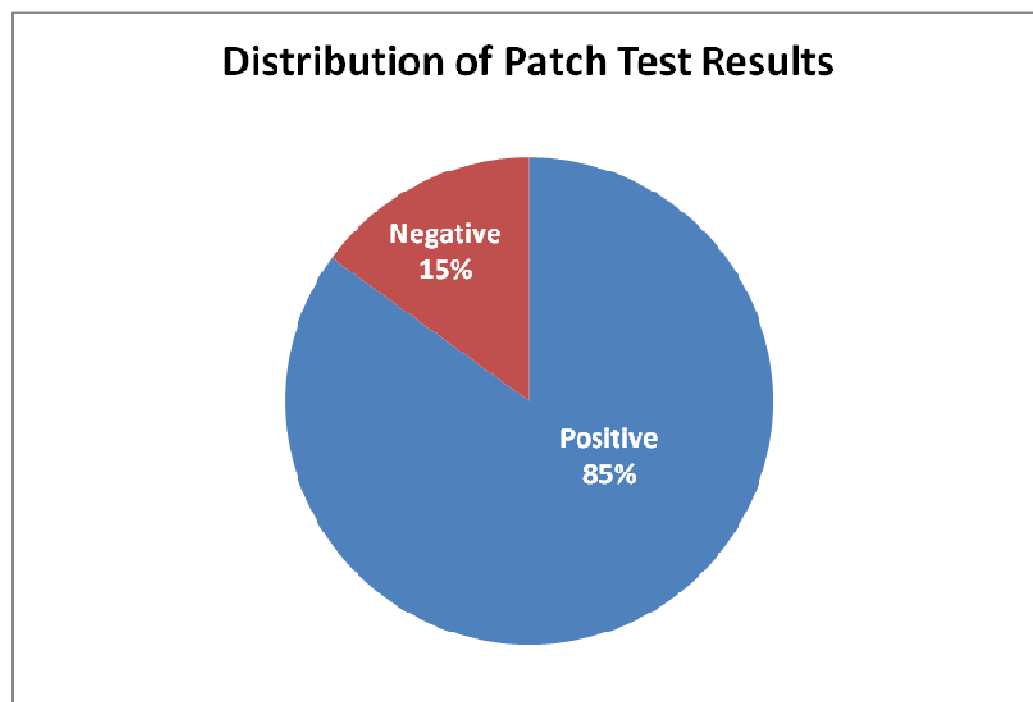


Figure -9

Table - 6**COSMETIC SERIES ALLERGENS POSITIVITY**

S. NO	ANTIGENS	NO OF PATIENTS (POSITIVE)	PERCENTAGE
01	Control	0	0
02	Hydroabietyl Alcohol	0	0
03	Amerchol L-101	1	5%
04	Benzyl Alcohol	0	0
05	Benzyl Salicylate	0	0
06	2-Bromo 2-Nitropropane-1, 3-Diol	0	0
07	2-Tert-Butyl-4-Methoxyphenol(BHA)	0	0
08	BHT	0	0
09	Cetyl Alcohol	0	0
10	Chloroacetamide	0	0
11	Chloroxylonol (PCMX)	0	0
12	Gallate Mix	7	35%
13	Geranium Oil Bourbon	0	0
14	Benzophenone-3	0	0
15	Drometrizole	0	0
16	Imidazolidinyl Urea	1	5%
17	Isopropyl myristate	0	0
18	Jasmine Absolute	2	10%
19	Lavender Absolute	1	5%
20	Musk mix	1	5%

21	Phenyl Salicylate	1	5%
22	Polysorbate 80	2	10%
23	Rosadamascena Extract	1	5%
24	Sorbic Acid	1	5%
25	Sorbitanoleate	1	5%
26	Sorbitan Sesquioleate	0	0
27	Stearyl alcohol	0	0
28	t-Butyl hydroquinone	1	5%
29	Thimerosal	1	5%
30	Triclosan	0	0
31	Triethanolamine	0	0
32	Vanillin	0	0
33	Oleamidopropyl Dimethylamine	0	0
34	Cetrimonium Bromide	6	30%
35	Jasmine synthetic	1	5%
36	Methenamine	0	0
37	Chlorhexidine digluconate	0	0
38	Phenyl Mercuric Acetate	0	0
39	Cocamidopropyl Betaine	0	0
40	Diazolidinyl Urea	0	0
41	Ethylenediamine Dihydrochloride	0	0
42	Quaternium-15	0	0
43	Propylene glycol	0	0
44	Methylisothiazolinone	0	0

	+Methylchloroisothiazolinone		
45	PPD	9	45%

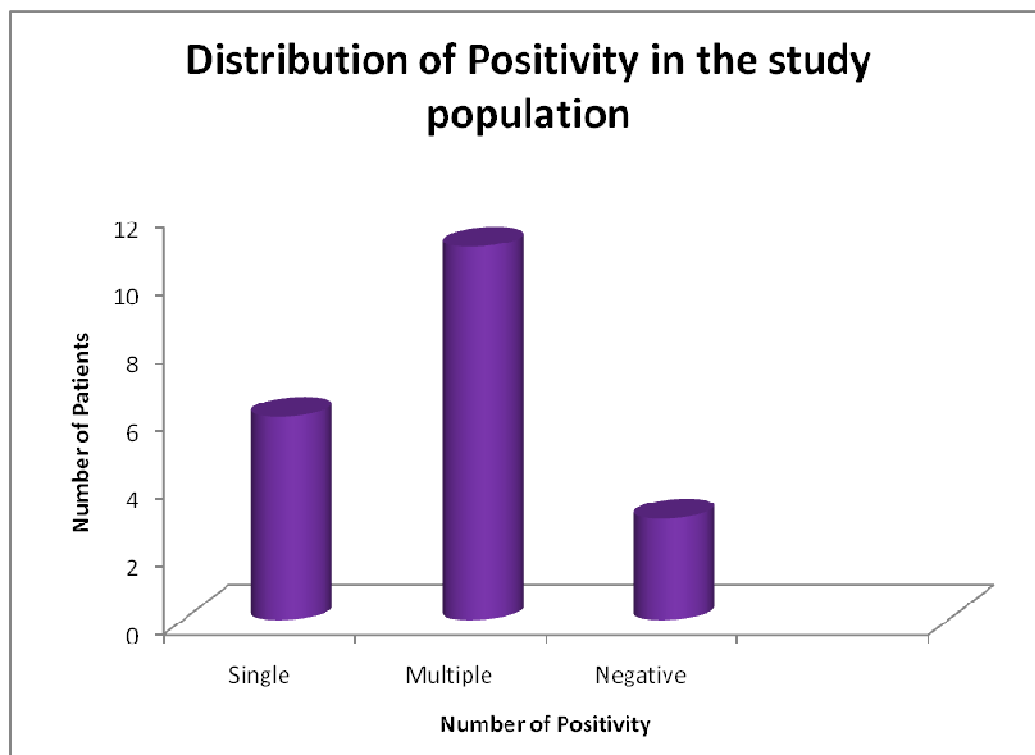


Figure - 10

Table - 7

FREQUENCY OF ALLERGENS POSITIVITY

S.NO	Frequency of number of allergens positive	No of patients	%
1.	One allergen positive	6	
2.	Two allergen positive	5	
3.	Three allergen positive	5	
4.	Four allergen positive	1	

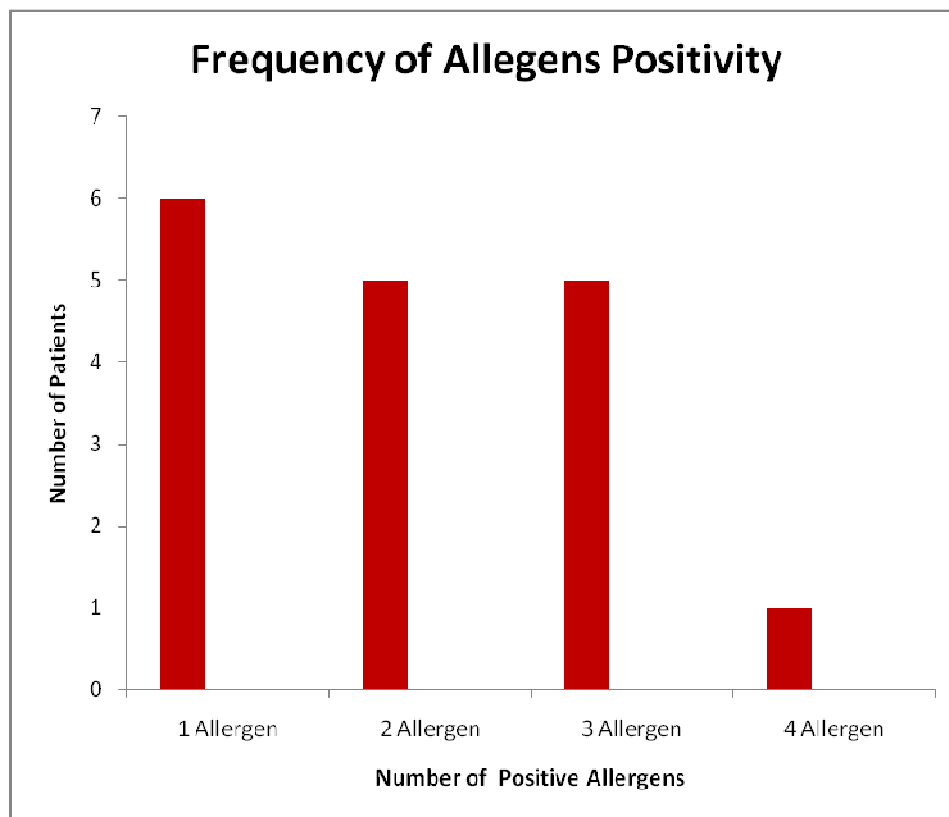


Figure - 11

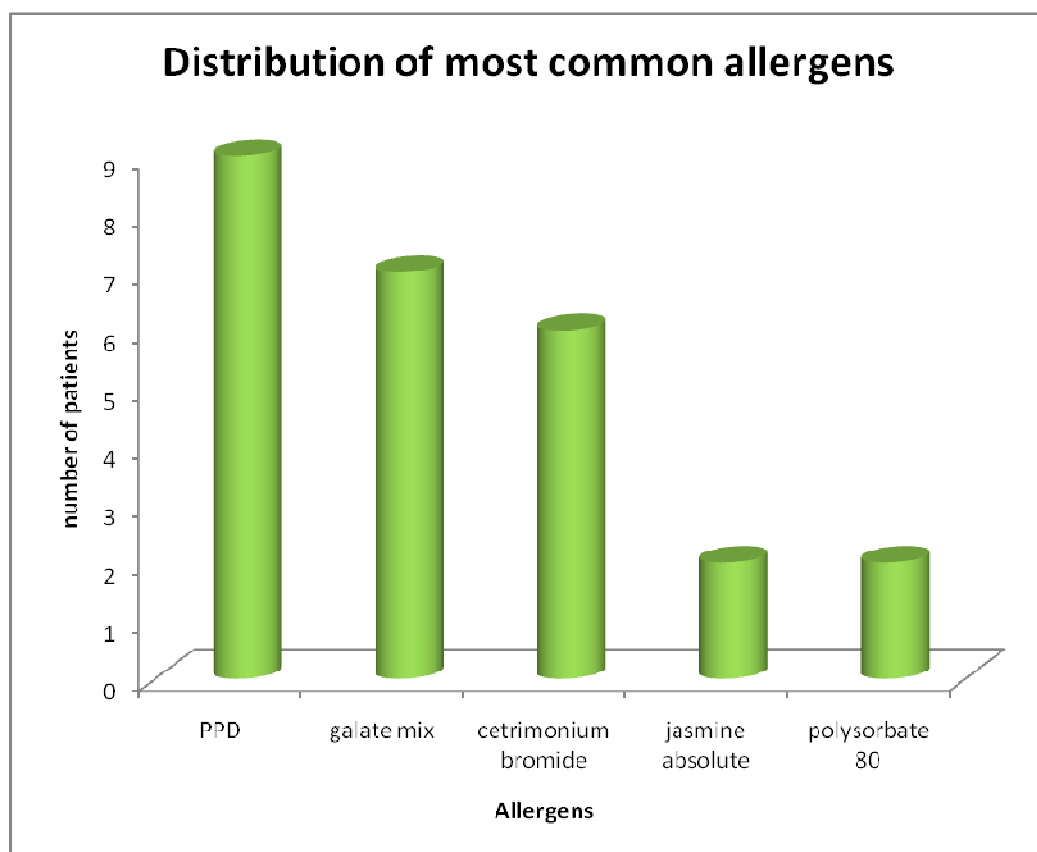


Figure - 12

DISCUSSION

Even though scalp pruritus is a common complaint, the number of patients consulting a dermatologist for this problem is very less. Only when it is intense and interferes with the quality of life, they consult the dermatologist

In our study, out of 20 patients , 9 were male and 11 were female, possibly due to the fact that women use more cosmetics compared to men. Similarly in various studies done for Allergic Contact dermatitis to cosmetics, there was female predominance.^{82,83,84,85}

In our study, we had patients with duration of scalp pruritus between 1 month to more than 1 year. Majority of them had scalp pruritus for 1-3 months duration, and 1 patient had a longer duration of more than 1 year.

Scalp pruritus was more common in the age group of 50-60 years (35 %) in our study, probably, because hair dyes are commonly used by people in this age group and PPD was the most common allergen. 25% of the patients belonged to the younger age group (20-30 years). They gave history of using multiple shampoos available under various brands in the market, advertising solutions for dry hair, normal hair, hair fall, repair etc. Therefore, they tend to change from one shampoo to another trying to find the suitable shampoo for their hair type.

In our study, 6 patients had associated dermatitis of scalp, 3 had preexisting dermatoses due to other causes, 2 had dermatitis due to the use of hair dyes and 1 patient was a known case of psoriasis with history of using hair dye. She had psoriatic plaque over the scalp.

Dermatitis due to cosmetic contact allergy has a peculiar pattern. Especially with hair dyes, the dermatitis is localized to the lateral area of the face®, but in our patients who had dermatitis, it was localized to the scalp.

Among the 20 patients tested, 17 patients (85%) had positive patch test whereas 3 patients (15%) had negative results. In patients with cosmetic dermatitis, the frequency of positive patch test reactions ranged from 76% to 85% in various studies. In our study, 85% had positive patch test results which is similar to other studies.

While testing with cosmetic allergens, doubtful reactions are clinically relevant in 44% of patients, whereas, 1+ & 2+ reactions are relevant in 80% of patients, more relevant when associated with stronger reactions of more than 2+. ⁸⁶ Hence it can be said that weak reactions may or maynot be relevant whereas strong reactions are most likely to be relevant. In our study, PPD had the highest reaction of 2+ and 3+, whereas, other allergens had 1+ positivity. All reactions that were doubtful on 48 hours reading were negative in the 72 hours reading. Although, doubtful reactions have minimal relevance, in our study, all the doubtful reactions were considered negative.

Hence, those allergens with minimal reactions could have caused the scalp pruritus in our patients.

In our study, the most common allergen was found to be PPD (9 out of 20 patients). However, 13 patients gave history of using hair dye for more than 2 years, but only 9 patients had a positive patch test reaction of more than 2+, which is very much significant. Positivity to hair dye is relevant in our patients because all these patients were using hair dye while consulting for pruritus.

According to the analysis of data of the information network of departments of dermatology in Germany, hair colouring agents were found to be the most common cause of scalp dermatitis.⁸⁷

In a recent study from 12 dermatology care centers, 2939 consecutive patients were subjected to patch testing to detect dye components and 4.5% were tested positive for PPD. In a study conducted by Dogra et al and Pasricha et al, the most common allergen was PPD in 35-42% of cases with very strong positivity.^{88,89} PPD containing temporary tattoo products such as black henna is also a triggering factor for allergic contact dermatitis.^{90,91}

The results are not surprising because of the significant increase in sensitization to PPD & other hair colouring agents like PTD (Para toluene diamine) & PAP (Para Amino Phenol).⁹²

The next common allergen was gallate mix which was positive in 35% of patients (7 out of 20). All the seven patients had 1+ positivity. In a study by Pramod et al.⁹³ gallate mix was found to be the most common allergen (40% of patients). A multicentric patch test study had shown that octyl gallate has more sensitizing capacity followed by dodecyl galate and propyl galate.^{94,95} Preservatives were found to be the second common allergens in cosmetic dermatoses. If the patient is positive for one particular component of gallate mix, they need not avoid all other components of the mix. Only the specific gallate which he or she reacted to should be avoided.⁵⁶

The next in line is cetrimonium bromide which was positive in 30% patients (6 out of 20) similar to the study done by Pramod et al,⁹³ which showed 28% positivity. These are surfactants used in shampoos and conditioners. In our study, 5 out of 6 patients positive to cetrimonium bromide gave history of using multiple shampoos and patch testing with all these products was difficult. It is possible that these patients might have used shampoos with cetrimonium bromide in the past which were not available while testing. However, 1 patient who was tested positive for cetrimonium bromide was using a shampoo that had cetrimonium bromide.

Jasmine absolute was positive in 2 out of the 20 patients (1 male and 1 female) and both patients had history of using jasmine scented hair oil.

In southern parts of India, women regularly adorn their hair with jasmine flowers from childhood as a part of their tradition. Interestingly, the female patient also gave history of adorning her hair with jasmine flowers regularly in addition to using jasmine scented hair oil which could have caused allergic contact dermatitis leading to scalp pruritus in this patient. So, a patch test with the jasmine flower could have been an adjuvant in the diagnosis.

Polysorbate 80 was positive in 2 patients. This is an auxillary emulsifier used in conditioners, particularly effective in providing emulsion stability that cannot be achieved by cationic agents.

Other allergens that had single positivity are amerchol L 101, imidazolidinyl urea, lavender absolute, musk mix, phenyl salicylate, rosadamascena extract, sorbic acid, sorbitanoleate, t-Butyl hydroquinone, thimerosal and jasmine synthetic.

Thiomerosal was positive in 5% (1 out of 20 patients) of our study group. Positivity to thiomerosal ranging from 1.6% to 37.6% has been reported in various studies.^{96,97,98} In a Polish study of children and adolescents with chronic dermatitis, it was found that thiomerosal sensitivity was reported in 11.7% (12 out of 103 children) and 37.6% (35 out of 93 adolescents).⁹⁸ Thiomerosal, which is a mercuric preservative, is an uncommon allergen and positivity to it may not be of relevance, as patient might have been exposed to this in the past.

Lavender absolute, jasmine synthetic and rosadamascena extract are fragrances which were tested positive only in 5% of our patients. Fragrances are reported to be the most common cause of contact dermatitis.^{99,100} However, in our study fragrances had the least positivity.

Even though fragrances are the commonest cause of contact allergy,^{24,25} it is difficult to identify and eliminate the ingredients, because the fragrances are considered trade secrets and manufacturing companies are not required to list the specific chemicals contributing to the aroma.¹⁰¹ Also, labelling of ingredients is complicated because there is a possibility that hundreds of different fragrance ingredients were mixed together to form that final fragrance in any given product. Hence, it becomes practically difficult to list out all the ingredients.

Whenever possible, patients were tested with their own products, (6 out of 20 patients) because a significant number of patients used multiple shampoos and they were not aware of the name of the products. One patient, when tested with his own product under dilution of 1:10 showed positive results. If a product is tested under improper dilutions, it can lead to false positive results, whereas, over dilution could cause false negative results, hence results can be misleading. This could be a reason for patch test negativity in our patients. Ingredients in cosmetics keep changing. In cosmetic industry change is constant, it's a rule not an exception. Also, there is a possibility of products that are non irritants under normal circumstances causing irritant reactions in a

closed patch test. Though, testing with patients' own products is essential, this is a challenging task.

In our study, PPD was the most common allergen. However, people possibly use hair dyes either once a month or on rare occasions, for hair that has grown after dying. PPD is the allergen that enters only the hair shaft but comes in contact with the scalp during application of the hair dye and can be washed off in approximately two hair washes. In contrast, shampoos were used more often by the patients in the study group and the allergens in the shampoos causing scalp pruritus are not common because PPD is a more potent allergen.

Our patients gave history of persistent pruritus even after changing shampoos multiple times. This can be explained by the fact that most of the shampoos have identical ingredients. When a person suspects a shampoo allergy, he/she tends to change over to another product that may also contain ingredients to which he or she is allergic. Hence, the pruritus does not subside and they may come to a misconception that the allergy is not due to the shampoo.

Many dermatologists do not prefer patch testing because it requires a lot of time, frequent visits to the doctor and suitable test materials are not easily available. However, patch testing can be very helpful in improving the patient's quality of life, if the allergen causing dermatitis is identified and avoided.

Rajagopalan et.al¹⁰² evaluated the cost effectiveness of patch testing in terms of quality of life in patients suspected to have allergic contact dermatitis and reported that patch test is a cost effective method and hence reduced the cost of therapy.

CONCLUSION

Scalp pruritus is a common complaint and a social embarrassment. Among the various causes of allergic contact dermatitis to hair cosmetics, could be a cause for scalp Pruritus. This study was undertaken to identify the allergen and the incidence of allergic contact dermatitis to topical preparations and cosmetics among patients with pruritus of scalp. In our study the most common allergen was found to be PPD, followed by gallate mix and cetrimonium bromide. In some of these cases allergic contact dermatitis may be responsible for the pruritus. However it is also possible that pruritus in some cases may be of past relevance and not the exact cause of present symptom.

We recommend patch testing in patients with long standing pruritus of scalp. However caution should be used before attributing pruritus to the allergy detected. Effort should be made to correlate the relevance of the sensitizer to the topical products used by the patient.

PATIENT INFORMATION SHEET

Center Name _____ Investigator
_____ Date _____

Name _____ Father's/ Husband's
Name _____

Age in years _____ Date of birth _____ Gender Male/
Female

Address _____

Religion Hindu/ Muslim/ Christian/ Sikh/ Jain/ Buddhist/ Parsi/ Others

Education Illiterate/ Primary/ Secondary/ Graduate/ Post-graduate

Family income (Rupees/month) <5000 / 5000-20000 / >20000

Cosmetics used	Frequency of application			
	Daily	2-3 times/ week	once/week	once in a while

Hair color

Hair gel

Perfumed hair oil

Conditioner

Shampoo

Perming

Straightening.

Hair spray

Any other

Presenting complaint

1. Dermatitis of scalp

4. Burning/ Stinging after application
5. Any other

Cosmetic series

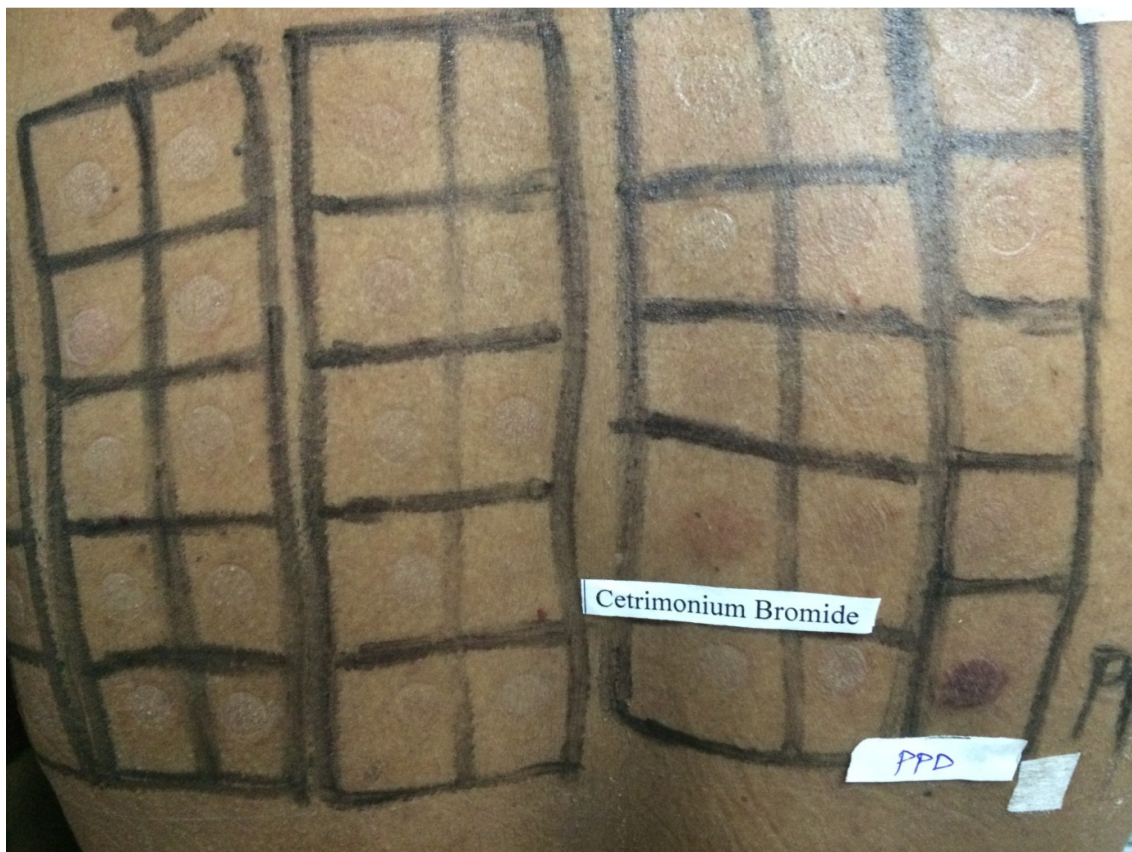
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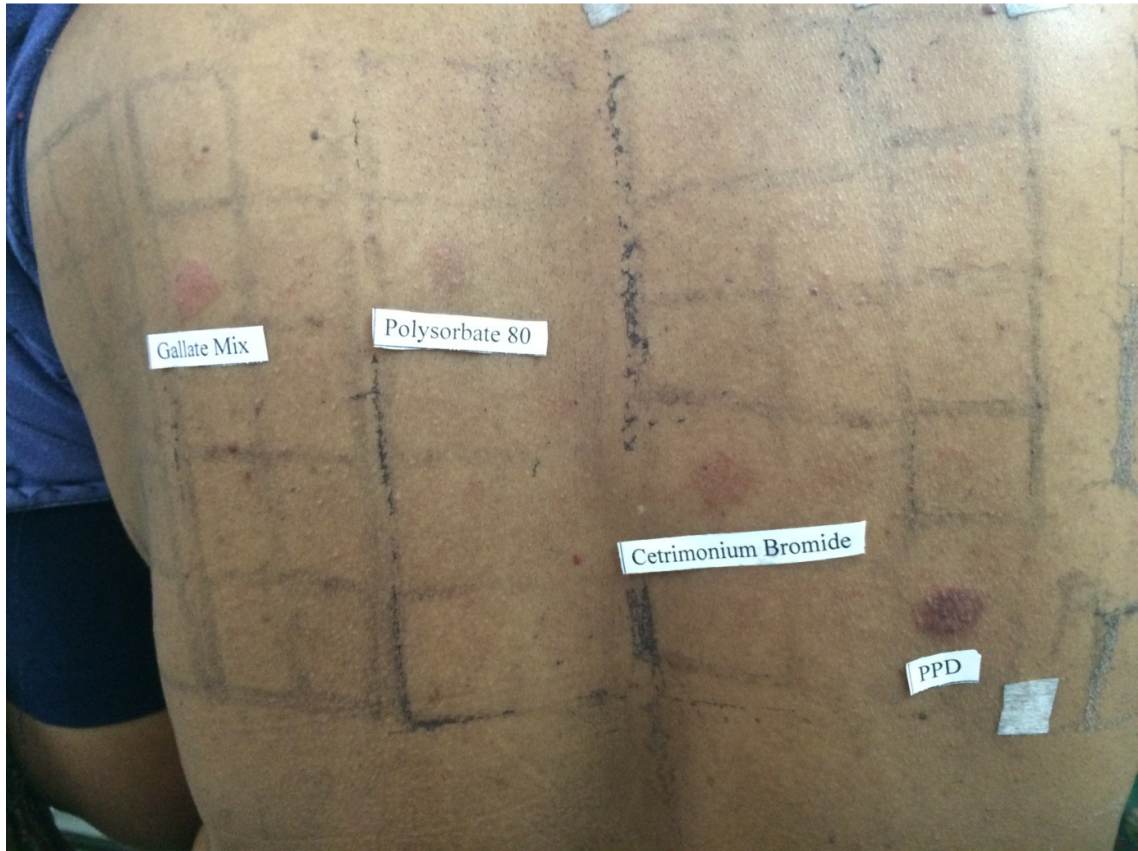
S.No.	ANTIGEN	%	Day	DAY
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				3	4	5
01	Control	100				
02	Hydroabietyl Alcohol	10				
03	Amerchol L-101	50				
04	Benzyl Alcohol	10				
05	Benzyl Salicylate	10				
06	2-Bromo 2-Nitropropane-1, 3-Diol	0.25				
07	2-Tert-Butyl-4-Methoxyphenol(BHA)	2				
08	BHT	2				
09	Cetyl Alcohol	5				
10	Chloroacetamide	0.2				
11	Chloroxyleneol (PCMX)	0.5				
12	Gallate Mix	1.5				
13	Geranium Oil Bourbon	2				
14	Benzophenone-3	10				
15	Drometrizole	1				
16	Imidazolidinyl Urea	2				
17	Isopropyl myristate	20				
18	Jasmine Absolute	2				
19	Lavender Absolute	2				
20	Musk mix	3				
21	Phenyl Salicylate	1				
22	Polysorbate 80	5				
23	Rosadamascena Extract	2				
24	Sorbic Acid	2				
25	Sorbitanoleate	5				
26	Sorbitan Sesquioleate	20				
27	Stearyl alcohol	30				
28	t-Butyl hydroquinone	1				

29	Thimerosal	0.1				
30	Triclosan	2				

31	Triethanolamine	2				
32	Vanillin	10				
33	Oleamidopropyl Dimethylamine	0.1				
34	Cetrimonium Bromide	0.5				
35	Jasmine synthetic	2				
36	Methenamine	2				
37	Chlorhexidine digluconate	0.5				
38	Phenyl Mercuric Acetate	0.01				
39	Cocamidopropyl Betaine	1				
40	Diazolidinyl Urea	2				
41	Ethylenediamine Dihydrochloride	1				
42	Quaternium-15	1				
43	Propylene glycol	5				
44	Methylisothiazolinone + Methylchloroisothiazolinone	0.02				
45	PPD					














Thimerosal

LIST OF ABBREVIATIONS

CGRP	Calcitonin gene related peptide
HF	Hair follicle
MC	Mast cells
PAR-2	Proteinase activating receptor 2
TRPV1	Transient receptor potential vanilloid-type 1
CBS	Cannabinoid receptors
NKRS	Neurokinin receptors
ET	Endothelin
ACD	Allergic contact dermatitis
PPD	para-phenylenediamine
ROAT	Repeated open application test
TRUE	Thin-layer rapid use epicutaneous test
MHC	Major histocompatibility complex
BHT	Butylated hydroxytoluene
PCMX	Chloroxylonol

MASTER CHART CODE

0	No, Negative
1	Yes, Positive
1-45	Cosmetic series allergens